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1972

ANNUAL REPORT
OF
PROGRAM ACTIVITIES

DIVISION OF RESEARCH RESOURCES

FISCAL YEAR 1972

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

ANNUAL REPORT

FISCAL YEAR 1972
(July 1, 1971-June 30, 1972)

DIVISION OF RESEARCH RESOURCES

National Institutes of Health
Bethesda, Maryland 20014

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REPORT OF THE DIRECTOR

Dr. Thomas G. Bowery

Report of the Division Director

Fiscal year 1972, represented a consequential period for the Division of Research Resources in terms of accomplishments not only of certain program goals and objectives, but also in striving to define and meet the significant human needs of the Division's personnel. As a result of Congressional action, budgetary increases were provided for most of our program elements. Additionally, the Senate directed us to initiate two new program activities; implementation of the Animal Welfare Act of 1970, and the institution of the Minority Schools Biomedical Support Program (MSBS). By the addition of these programs to the Division's repertoire of support mechanisms, we are better able to respond to the needs of the biomedical research community. With respect to the latter program (MSBS), the Division is proud to have been able to provide the NIH leadership in launching a viable and visible program aimed specifically at minority institutions.

Despite budgetary increases for most of our programs, new resource development or expansion has been negligible since the increases have in most cases been barely able to offset inflationary factors. By the very nature of resources, with large budgetary items such as hospitalization, the inflationary spiral has well exceeded cost-of-living increases in our budgets. Only through prudent fiscal management and funding of non-competitive awards at less than Council recommended levels have our program administrators been able to initiate a few new efforts. The problem has been so serious that potential applicants are becoming too discouraged to submit proposals. In both the Biotechnology Resources Program and the General Clinical Research Centers Program, fewer than three new centers have been funded in recent years. The General Research Support Grant and Biomedical Sciences Support Grant Programs have again faced a year of decreased funding due to a stable budget in the face of increased eligibility. The biomedical research community is becoming increasingly concerned at the gradual erosion of these funds.

In respect to the human needs of the Division, fiscal year 1972 has been the most critical one in the history of the DRR. Although I have eagerly endorsed and promoted official NIH pronouncements concerning Upward Mobility, Equal Employment Opportunity, special training programs, etc., it has become next to impossible to achieve these goals when faced with the serious constraints and restrictions imposed on promotions through grade de-escalation and position reduction. Not only is my "credibility" questioned, but the morale of the whole Division is suffering.

Positively, we have been successful in recruiting two minority professionals, four employees are enrolled in the Upward Mobility College, and three others are pursuing college credit at outside universities. Our percentage of minority employees has increased during the year and we fully anticipate this trend to continue. The Division has recently held a three-day EEO conference, in which over 80 percent of the Division participated.

Paramount among the concerns identified at this conference was (1) the need for better communication and understanding between supervisors and fellow workers; and (2) our inability to achieve better minority representation at the higher grade levels due to restrictions on hiring and promotions.

Despite the fact that this Division was charged with the initiation of two highly important and visible programs, no additional staff was permitted; indeed the Division suffered one of the largest personnel cuts within the entire NIH -- close to ten percent. I have every confidence in the ability of my staff and their willingness to assume increasing workloads. However, I cannot, nor can NIH, expect this level of sustained output to continue much longer without a loss in quality.

I sincerely hope that fiscal year 1973, will see an improvement in our capability to more effectively respond to the programmatic and human needs of the Division.

DRR BRANCH REPORTS

Fiscal Year 1972
ANNUAL REPORT
Biotechnology Resources Branch
Division of Research Resources

INTRODUCTION

The nationwide array of NIH-supported Biotechnology Resources is unsurpassed as a medium through which the physical sciences, mathematics, and engineering can influence--and be influenced by--the domain of biomedicine. Biotechnology Resources create conditions under which the most sophisticated, health-relevant forms of digital computation, mass spectrometry, nuclear magnetic resonance spectroscopy, electron microscopy, and biological materials preparation are spawned and evaluated in the full context of the biomedical world. These centers of technological excellence frequently offer the clientele of the NIH's categorical programs investigative opportunities which otherwise would not be available to them.

The nature and scope of the various Biotechnology Resources follow closely the major technological advances occurring both inside and outside the biomedical research community. Beginning from the almost pure service activities ten years ago, the program has evolved to the point where, in addition to the service feature, each resource now (a) performs core research and development in its own area of technology, (b) enters into close collaborative activities with its user community, and (c) conducts formal and informal training to acquire new skills for its own staff and to diffuse the benefits of its technology to its user community. By incorporating all four of these activities within a resource, the people who run them can provide almost immediate response to the needs of the resource users. This report summarizes the status of the Biotechnology Resources' endeavors in Fiscal Year 1972.

BASIC DATA ON THE BIOTECHNOLOGY RESOURCES PROGRAM

Types of Biotechnology Resources

That the pattern of supported Biotechnology Resources and the type of assistance they provide the research community are highly varied is shown by the fact that the 51 currently active grants and 4 currently active contracts are classified as follows:

33 computer resource grants
2 resource-related project in computer science
1 computer graphics evaluation contract
11 biochemistry instrumentation resource grants
1 mass spectrometry services contract
2 electron microscopy resource grants
1 electron microscopy services contract
3 biological materials resource grants
1 fast-reaction kinetics services contract

The aggregate annual expenditure level for these activities is approximately $11 million. A listing of the BRB-sponsored activities active at this writing is given in Table I.

It is particularly interesting to view the foregoing data in historical perspective. In 1967, for example, the program supported 61 resources at a cost of $12.2 million. These resources fell into the following categories:

48 computer resources
10 biochemistry instrumentation resources
3 biological materials resources

While the numbers of each type of resource have not changed greatly during the intervening years, their substantive nature has, especially in the computer resource category. Compared to the 28 batch-processing or off-line, general-purpose computer installations in 1967, the program will have only 1 resource of this type by 1974. Whereas in 1967 there were 15 computer resources concerned primarily with on-line, real-time interactive use, now there are 21. There seems to be little doubt that the ever more sophisticated computational needs of biomedical scientists are best met by highly specialized resources and not general-purpose ones.

Rapid and far-reaching change is not limited to the computer resource category. For example, as the requisite talent becomes available to manage mass spectrometers in a variety of biomedical settings, there is a strong trend toward the use of these instruments in clinical investigation, especially in pediatric research. It is also of interest to note that, unlike even a few years ago, all of the biochemistry instrumentation resources now contain a dedicated computer for reduction of data to a manageable form. Similarily, almost exclusively as a result of efforts by the Biotechnology Resources Program in the past several years, high voltage (i.e., one million volt) electron microscopy services have become a reality in the United States and are now being applied for such purposes as obtaining stereo micrographs of thick-sectioned biological material and examining the surfaces and contacts of intact wet cells in a hydration chamber.

The "new funding" actions of the Biotechnology Resources Program during Fiscal Year 1972 contributed further to this diversification. At this writing it appears that four new resources or resource-related research projects will have been launched in the July 1, 1971-June 30, 1972, period: two nuclear magnetic resonance resources, each involved with a wide-ranging set of basic science and clinical research users; one computer resource specializing in direct interaction with biochemical investigators on their experiments; and one research project involving low cost, remote computer graphics and radio frequency communications technology. Heterogeneity and specialization continue to be hallmarks of the Biotechnology Resources Program.

Support of Categorical Programs

One of the primary measures of accomplishment that can be applied to the Biotechnology Resources Program is the extent to which its sponsored

activities markedly assist the various NIH categorical programs. With their cadres of highly skilled staff scientists and their specialized and often unique facilities, Biotechnology Resources are frequently the scene of productive encounters between experts in a given technology and experts in a given medical discipline. Table II gives additional insight into the breadth and depth of this program on the health research supported by the DHEW. Numbers represent in thousands of dollars the amount of grant support of users of Biotechnology Resources by source of support with the Public Health Service. Table III represents support within the NIH.

The distribution of research assisted by this program is not uniform but does reflect, in part, how apportionment of research funds to the NIH institutes and other agencies brings research talent to a given area and how the staff of the Biotechnology Resources respond in meeting these demands. Computer and biochemistry instrumentation resources are making significant levels of contribution to life sciences research supported outside the NIH. The data presented in these tables was acquired from annual reports submitted by 24 computer resources, 10 biochemistry instrumentation resources, 3 biomaterials resources, and 2 electron microscopy resources.

MAJOR PROGRAM DEVELOPMENTS DURING FISCAL YEAR 1972

High Voltage Electron Microscopy

During the past year, the efforts of the Biotechnology Resources Program to assess the biomedical research utility of one million volt electron microscopy technology reached an important milestone. As described in previous annual reports, access for biomedical scientists to the one million volt instrument at the United States Steel research laboratories in Monroeville, Pennsylvania (until recently the only one of its kind in the Nation) has been made possible by a BRB contract. In November of 1971, the several major groups of scientists who have been taking advantage of the contract-subsidized services assembled, along with BRB staff and advisors, for a two-day meeting at the instrument site. Through a broad spectrum of research reports and in-depth discussions, these investigators clearly defined the promises and the problems of this new technology. Their initial findings--and their subsequent efforts in using the microscope--not only represent potentially significant contributions to the improved morphological characterization of muscle fibers, chromosomes, viruses, teeth, and other biological materials, but also will place future BRB efforts in this area on a firmer base. For example, the experiences of microscope users, BRB staff, and advisors involved with the U.S. Steel contract activities will almost certainly influence the domain of scientific applications and the style of operations selected for the BRB-supported one million volt facilities at the Universities of Wisconsin and Colorado which are scheduled to go into full operation in Fiscal Year 1973.

Clinical Research Applications of Computer Technology

Fiscal Year 1972 also saw the emergence of a major new program effort involving both the BRB and the General Clinical Research Centers Branch and focusing on the potential utility of computer technology in support of human clinical investigation. Beginning in July 1971 with a DRR-organized conference attended

TABLE I

BRB SPONSORED ACTIVITIES AS OF 5/26/72

Number	Principal Investigator	Institution	Title
COMPUTER			
RR-3	Wilfrid J. Dixon, Ph.D.	University of California, Los Angeles, California	Health Sciences Computer Resource
RR-7	Earl H. Wood, M.D.	Mayo Foundation, Rochester, Minnesota	Computer Processing in Biomedical Systems
RR-11	David D. Mason, Ph.D.	North Carolina State University, Raleigh, North Carolina	Computer Use in the Health Sciences
RR-12	Homer R. Warner, M.D.	University of Utah, Salt Lake City, Utah	Computer Facility for Medical Community
RR-13	Richard H. Earle, M.D.	University of Chicago, Chicago, Illinois	Computer Facility for Medical Community
RR-15	Martin Pring, Ph.D.	University of Penn., Philadelphia, Penn.	Medical School Computer Facility
RR-16	S. James Kilpatrick, Jr., Ph.D.	Medical College of Virginia, Richmond, Virginia	Support of Scientific Computation Laboratory
RR-145	Josiah Macy, Jr., Ph.D.	University of Alabama Medical Center, Birmingham, Alabama	Use of Electronic Computers in Health Research
RR-241	John J. Osborn, M.D.	Institute of Medical Sciences, San Francisco, California	Development of a Biomedical Research Data Facility
RR-249	Joseph E. Hind, Ph.D.	University of Wisconsin, Madison, Wisconsin	Support of Laboratory Computer Resources
RR-254	Richard T. Eastwood, Ph.D.	Texas Medical Center, Inc., Houston, Texas	Regional Computer Facility
RR-267	Eugene Ackerman, Ph.D.	University of Minnesota, Minneapolis, Minnesota	Health Computer Resource

RR-276	Ivan R. Neilsen, Ph.D.	Loma Linda University, Loma Linda, California	Development of Biomedical Computation Facility
RR-291	Arthur Rosen, M.D.	Research Foundation of State University of New York, Albany, New York	Biomathematical Computer Research Center
RR-311	Joshua Lederberg, Ph.D.	Stanford University, Stanford, California	Advanced Computer for Medical Research (ACME)
RR-326	Cyril L. Comar, Ph.D.	Cornell University, Ithaca, New York	Computer Research Resource
RR-353	William J. Mueller, BSE	Research Foundation of State University of New York, Albany, New York	Research Data Processing Center
RR-370	Herbert M. Teager, SCD	University Hospital, Boston, Massachusetts	Medical Computer Resource
RR-374	Theodore H. Kehl, Ph.D.	University of Washington, Seattle, Washington	Support for Physiology and Biophysics Computer
RR-396	Jerome R. Cox, Jr., DSC	Washington University, St. Louis, Missouri	A Resource for Biomedical Computing
RR-417	Richard G. Cornell, M.D.	University of Michigan, Ann Arbor, Michigan	A Development Program for Biomedical Computing
RR-442	Cyrus Levinthal, Ph.D.	Columbia University, New York, New York	Computer Resource for Image Processing and Displays
RR-443	Robert Nathan, Ph.D.	California Institute of of Technology, Pasadena, California	A Computer Resource for Pictorial Data Processing
RR-452	Sidney Katz, Ph.D.	Medical University of South Carolina, Charleston, South Carolina	Research Data Processing Center
RR-576	George T. Harrell, M.D.	The Pennsylvania State University, Hershey, Pennsylvania	Biomedical Computing Resource

RR-578	Robert Langridge, Ph.D.	Princeton University, Princeton, New Jersey	Special Research Resource for Biomolecular Graphics
RR-643	Saul Amarel, D.E.	Rutgers University, New Brunswick, New Jersey	Biotechnology Resource: Computers in Biomedicine
RR-757	Joseph Kraut, Ph.D.	University of California, La Jolla, California	Implementation of a Laboratory Automation System

RESOURCE-RELATED RESEARCH PROJECTS

RR-667	Harold W. Shipton, C.E.	University of Iowa, Iowa City, Iowa	A Biomedical Computer Terminal System
RR-612	Edward A. Feigenbaum, Ph.D.	Stanford University, Stanford, California	Resource-Related Research Computers and Chemistry

BIOCHEMISTRY INSTRUMENTATION RESOURCES

RR-273	Richard Abrams, Ph.D.	University of Pittsburgh, Pittsburgh, Pennsylvania	Mass Spectrometric Facility for Biomedical Research
RR-292	Aksel A. Bothner-By, Ph.D.	Mellon-Pittsburgh-Carnegie Corporation, Pittsburgh, Pennsylvania	NMR Facility for Biomedical Studies
RR-317	Klaus Biemann, Ph.D.	Massachusetts Institute of Technology, Cambridge, Massachusetts	Mass Spectrometry Facility for Biomedical Research
RR-328	Jules B. LaPidus, Ph.D.	Ohio State University Research Foundation, Columbus, Ohio	An NMR Facility for Biomedical Research
RR-330	Monroe E. Wall, Ph.D.	Research Triangle Institute, Research Triangle Park, North Carolina	Mass Spectrometry Center for Research Triangle Region
RR-355	Jerrold Meinwald, Ph.D.	Cornell University, Ithaca, New York	High Resolution Mass Spectrometer Facility
RR-356	Seymour R. Lipsky, M.D.	Yale University, New Haven, Connecticut	Continuation of Physical Sciences Instrument Facility

RR-480	Charles C. Sweeley, Ph.D.	Michigan State University, East Lansing, Michigan	Support of Michigan State Mass Spectrometer Facility
RR-542	Mildred Cohn, Ph.D.	University of Penn., Philadelphia, Penn.	220 MC NMR Spectrometer Facility
RR-574	David M. Grant, Ph.D.	University of Utah, Salt Lake City, Utah	Regional Research Facility in NMR
RR-636	Harry Eagle, M.D.	Albert Einstein College of Medicine, Bronx, New York	Biotechnology Resource for NMR Studies of Biomolecules
ELECTRON MICROSCOPY			
RR-570	Hans Ris, Ph.D.	University of Wisconsin, Madison, Wisconsin	Electron Microscope Facility for Biomedical Research
RR-592	Keith R. Porter, Ph.D.	University of Colorado, Boulder, Colorado	High Voltage Electron Microscopy of Biological Systems
BIOMATERIALS			
RR-117	William A. Clark, Ph.D.	American Type Culture Collection, Rockville, Maryland	Preservation of the American Type Culture Collection
RR-226	John C. Garver, Ph.D.	University of Wisconsin, Madison, Wisconsin	Biochemistry Pilot Plant
RR-346	Henry G. Mautner, Ph.D.	Tufts University, Boston, Massachusetts	New England Enzyme Center
CONTRACTS			
NIH 71-444	Fred Kayne	Johnson Foundation, University of Penn., Philadelphia, Penn.	Study of Fast Reaction Biomedically Relevant Chemical Systems
NIH 71-2483	Rodger L. Foltz, Ph.D.	Battelle Memorial Institute, Columbus, Ohio	High Resolution Mass Spectrometry Service
NIH 70-4128	Harold Shipton, C.E.	University of Iowa, Iowa City, Iowa	Construct and Assemble Eight General-Purpose Graphics Terminals

NIH 70-4136	Robert M. Fisher	U.S. Steel Engineers and Consultants, Inc., A Subsidiary of U.S. Steel Corporation, Pittsburgh, Pennsylvania	Access health scientists to the high voltage electron microscope located in the Edgar C. Bain Laboratory for Fundamental Research, Monroeville, Penn.

TABLE II

BIOTECHNOLOGY RESOURCES BRANCH

AMOUNT OF GRANT SUPPORT OF USERS OF BIOTECHNOLOGY RESOURCES
BY SOURCE OF SUPPORT, EXCLUDING DRR FUNDS, AND RESOURCE
FUNDS FOR FY 1972 IN THOUSANDS OF DOLLARS
(NUMBER OF GRANT PROJECTS SERVED BY RESOURCES)

FUNDING INFORMATION PROVIDED IN 39 BRB ANNUAL REPORTS
(PROJECT INFORMATION PROVIDED IN 26 BRB ANNUAL REPORTS)

	PUBLIC HEALTH SERVICE					
Type of Resource	NIH	BHME	NLM	EHS	HSMHA	TOTAL
Computer	$27,548	$245	$298	$261	$8,842	$37,194
Biochemistry Instrumentation	3,526				1,124	4,650
Biomaterials	1,942					1,942
Electron Microscopy	900*					900*
TOTAL FUNDING	$33,916	$245	$298	$261	$9,966	$44,686
(TOTAL PROJECTS)	(390)	(34)	(41)	(35)	(106)	(606)

*Estimated

TABLE III

BIOTECHNOLOGY RESOURCES BRANCH

AMOUNT OF GRANT SUPPORT OF USERS OF BIOTECHNOLOGY RESOURCES
BY SOURCE OF SUPPORT, EXCLUDING DRR FUNDS, AND RESOURCE
FUNDS FOR FY 1972 IN THOUSANDS OF DOLLARS
(NUMBER OF GRANT PROJECTS SERVED BY RESOURCES)

FUNDING INFORMATION PROVIDED IN 39 BRB ANNUAL REPORTS
(PROJECT INFORMATION PROVIDED IN 26 BRB ANNUAL REPORTS)

NATIONAL INSTITUTES OF HEALTH

Type of Resource	AI	AM	CA	DE	ES	EY	GM	HD	HE	NS	TOTAL
Computer	$ 889	$1,833	$2,505	$1,019	$ 37	$463	$6,745	$3,155	$7,155	$3,747	$27,548
	(13)	(32)	(27)	(3)	(1)	(1)	(74)	(33)	(46)	(40)	(270)
Biochemistry Instrumentation	333	533	500		139		1,428	132	394	67	3,526
	(9)	(15)	(17)		(1)		(27)	(2)	(12)	(3)	(86)
Biomaterials	216	465	541				603	117			1,942
	(6)	(7)	(7)				(12)	(2)			(34)
Electron Microscopy	(Not available - 22 grants are using U.S. Steel HVEM under DRR Contract)										
TOTAL FUNDING	$1,438	$2,831	$3,546	$1,019	$176	$463	$8,776	$3,404	$7,549	$3,814	$33,016
(TOTAL PROJECTS)	(28)	(54)	(51)	(3)	(2)	(1)	(113)	(37)	(58)	(43)	(390)

by both computer and clinical research experts, DRR staff were able to specify a long-range series of endeavors, involving both grants and contracts, through which the role of automated information-handling in the clinical research world might be fully and accurately characterized. One of the earliest of these endeavors is a coordinated array of four contracts designed to bring three General Clinical Research Centers and one computer technology organization together into a consortium with DRR staff and advisors for the purposes of analyzing the processes of clinical investigation and identifying their potentially viable points of intersection with computer technology. At this writing, the members of the consortium are being selected through competitive review process and are scheduled to begin work late in Fiscal Year 1973. The consortium's results are expected to become the primary basis upon which future contractual efforts are designed and executed.

STATUS OF SCIENTIFIC PROGRAMS

Computer sciences and technology are now capable of interacting with the biomedical researcher in extending his investigative sensors in ways not possible without this technology. The computer resources supported under this program have developed, among other things, operating systems which:

-- monitor and predict, through models, potential faults in life-support equipment such as is found in cardiopulmonary intensive care units (Institute of Medical Sciences, San Francisco; University of Utah)

-- place major discrete health care and clinical research functions such as radiation treatment planning and nuclear medicine applications under nearly comprehensive computer control (Washington University, St. Louis)

-- provide routine on-line control of experiments (University of Wisconsin; University of Utah, Latter-Day Saints Hospital; Cornell University; Stanford University; University of Washington; Washington University; Mayo Foundation)

-- extend the investigator's ability to cope with vast and complex data through direct interation with computers (Columbia University; UCLA)

-- permit the investigator to control an experiment in terms of planning, experimental design, hypothesis formation, management and perusal of personal files, analysis and communications of data, retrospective search of data, and help him make more effective use of the research environment (Stanford University; UCLA; Baylor College of Medicine)

-- make it quicker to bring mini-computers into action in specialized research applications (Stanford University; University of Pennsylvania; Baylor College of Medicine)

-- permit the biochemist to see his data in terms of chemical structure and molecular conformation as opposed to data in numerical form (Princeton University; Washington University; Columbia University)

-- provide image enhancement and processing techniques that offer an approach to 1Å in resolution for electromicroscopists (Jet Propulsion Laboratory)

-- provide techniques of artificial intelligence in support of an array of modeling and problem-solving problems spanning several biomedical disciplines (Rutgers University)

High resolution nuclear magnetic resonance spectroscopy has opened new vistas in medical research. As a result of increased resolving power, much more detailed structural information can now be obtained on large, complex molecules than is possible using other more conventional techniques. This technology has made a major impact on our understanding of enzymes, their structure and function.

Examples:

-- high resolution NMR has made it possible for scientists to examine the enzyme, ribonuclease A, in sufficient detail to determine the three-dimensional structural features that are necessary for enzyme activity (Mellon-Pittsburgh-Carnegie Corporation)

-- differences in the three-dimensional structure of the sugar portion of DNA and RNA have been observed as part of an investigation into the function of these important constraints of biological systems (University of Pennsylvania)

Mass spectrometry has become a vital analytical tool in biomedical research. Advancements such as chemical ionization mass spectrometry, improved methods for automatic data collection and processing, and increased instrument sensitivity have made it possible to determine the structure of many compounds obtained from biological sources that are available in only submicrogram amounts.

Examples:

-- mass spectral analysis of extracts of the inner walls of human arteries from patients suffering from arteriosclerosis has led to the identification of a number of components in deposits resulting from this disease (MIT)

-- procedures are being developed for analyzing microgram quantities of peptides to determine their amino acid sequences (Cornell University)

-- procedures are being developed for analyzing substances of exceedingly low volatility by mass spectrometry (Yale University)

-- mass spectrometry is being used in the structure elucidation of biologically active substances isolated from natural sources in small quantities (Research Triangle Institute)

High voltage electron microscopy (one million volt) enables three-dimensional observations to be made of thick-sectioned biological material, thus extending investigations on complex structures such as those found in chromosomes, muscles, and the internal organization of the brain.

PROGRAM EVALUATION AND PLANNING ACTIVITIES

Program Efforts

Two program issues received particular attention during the past year: (a) program analysis and evaluation, and (b) future problems predicted to arise in resource sharing by institutions. While initial and periodic review by the Initial Review Groups and Council provide a measure of the scientific merit and effectiveness of Biotechnology Resources, program responsibilities require careful attention to the rate of diffusion of biotechnology into biomedical research; the cost effectiveness of serving that community; and the mechanism of the most effective disposition of existing, but untapped, resource capability available to and needed by the Nation's biomedical researchers. Assessment and evaluation studies of computer resources are greatly facilitated by the ease of programming to produce self-monitoring and accounting data. The annual reports provide a great amount of data acquired directly from such programs. The staff of the BRB is conducting a study using this data and other information to gain deeper insight into present and future program trends and to avoid future deficiencies by developing appropriate operational and support mechanisms.

The Rate of Diffusion of Computer Technology into the Research Community

One metric which has been developed has predictive properties regarding the development of certain resources. This measure is the ratio of productive computer hours logged by the user community of the resource to the number of full-time equivalents of programmers on the resource staff for a given year. The technical skill and interpersonal attitudes of the programmer staff seem to be important, along with the ability of the Principal Investigator to create and implement a hardware/software system matching the needs of his user community. Retrospective examination of this ratio confirms its effectiveness not only as a measure of the rate of diffusion of computer technology; but also, when combined with a cost metric (e.g., see below), it serves as a pointer to the viability of a resource relative to the review system. Attempts to rationalize this diffusion measure keep returning, in part at least, to the subjective aspects of resource operations.

Costs of Serving the Biomedical Research Community

Since it is now clear that the BRB Program can best serve the biomedical research community by encouraging the development and use of specialized resources, it is more important than ever to assess the relative costs of specialization and generality. Measures of total costs to create both generalized and specialized centers has, interestingly enough, shown little difference; and, in most cases, those computer systems especially developed for the research community are less costly than general-purpose ones, i.e., utilization by the research community is much higher when their needs are addressed directly by the staff and system of a Biotechnology Resource.

BRB interests in cost measures stem from the programmatic goal of seeing that biomedical computer technology contributes to an optimal way within the funds available. The strategy has been to create and nurture resources and then see them sustained without further BRB funds. Costs obviously play an important role here, for if a resource is to become self-sustaining, it must be able to compete for computing dollars within its own environment. Thus, a cost measure such as total production time in hours per year divided by the average annual BRB award dollars per year gives a measure through the BRB-support stages. Average annual amounts are used to cover rental/purchase variations introduced by alternative procurement methods selected by the grantees. Total computer production time is the total core research and user time interacting directly with the computer as is indicated in the annual resource usage summaries, i.e., total man/machine interaction time.

When this cost measure and the above diffusion measure are graphed and examined together for a single resource, year-by-year changes show the development of that resource in time.

When the diffusion metric and cost metric are plotted for the computer resource program and priority scores from the initial reviews (Figure 1) are included, a general separation of resources into successful and unsuccessful sustained support is observed. Should this observation prove to be consistent in time, it can become a valuable management tool for this program.

When taken separately over the entire computer resource program, the cost measure shows the effectiveness in moving from batch-processing systems to specialized systems developed for specific research needs, as shown in the cost/effectiveness metric during the years 1968-71.

BRB Dollars Per Computer Production Hour	1968	1969	1970	1971
	$91/hr.	$70/hr.	$72/hr.	$52/hr.

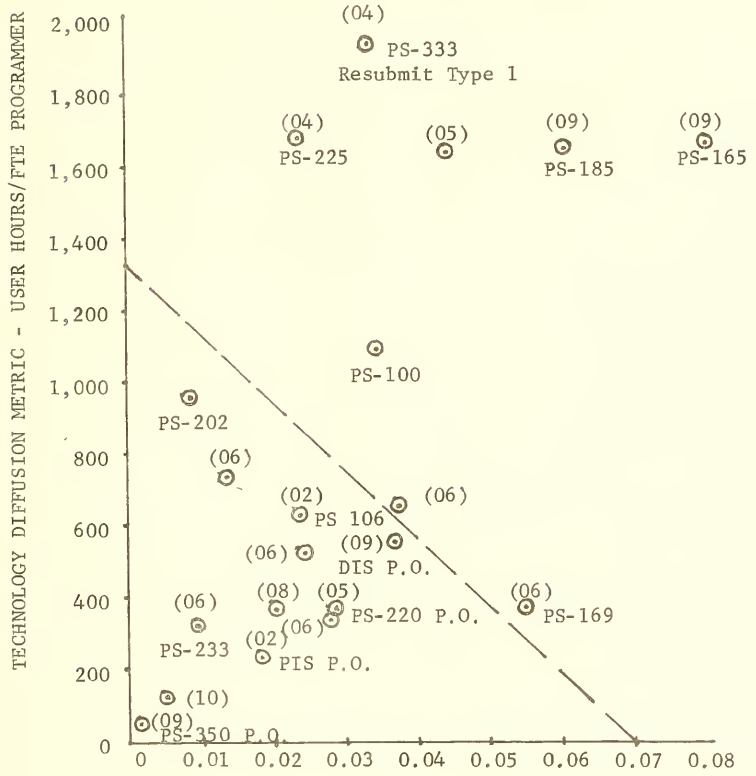
Utilization of Existing, Untapped Computer Capability by the Research Community

Assessment of existing, untapped computer capacity in a life sciences setting and the potentiality for more effective machine utilization is a task for which the traditional notions about conventional computer-in-service operations are of little use. Today's conception of a Biotechnology Computer Resource has grown from the pure service activities ten years ago to highly specialized

FIGURE 1

OBSERVATION OF PRIORITY SCORES (1972)
AND EFFECTIVENESS MEASURES

PS - Priority Score
( ) - Grant Year
P.O. - Phase Out Recommended by Study Section
- Resource Trend



COST EFFECTIVENESS METRIC -
TOTAL COMPUTER PRODUCTION HOURS/ANNUAL AVERAGE BRB DOLLARS

systems devoted to the specific needs of local research. In addition to the service role, now each resource performs core research and development in its own area of technology; enters into close collaborative activities with its user community; and conducts informal training related to the diffusion of computer technology into biomedical research. Biotechnology Resources have many features that must be observed in determining what style and level of system utilization is optimal towards the program goals.

Since these resources exist and are operated for the human researcher and interact intimately with him, it is not realistic to expect this user community to interact with the computer seven days each week. However, since the resource subserves the user here, it must be on call at his demand, i.e., during his working periods. Thus, the resources are developed to handle the needs peaking during the working day but offering access to the computer during off-peak working periods. The pattern of reported usage by the day and year confirms this notion.

These factors, together with perceived needs of today's biomedical researchers and projected needs of the next generation of biomedical researchers, clearly demonstrate that more attention will need to be focused on resource sharing, not just in a localized region, but across the country. These needs, already satisfied locally in some of the BRB resources, can be served by specifically developed biomedical computer resources in the following areas:

1. simulation techniques;
2. file processing;
3. numerical computation;
4. non-numerical manipulation;
5. remote, on-line data gathering;
6. remote, on-line digital control of experiments; and
7. building of special health sciences information bases.

As the technology of computer networks becomes fully developed, it will be realistic within the next decade to consider sharing of specialized biomedical computer resources among the users by a computer network. It is unlikely that the initiative in developing this network will come solely from the grantee community, for there is very little incentive for one institution to expand its skills in a way that largely benefits scientists not related to it. Also, it is not known that geographically separate institutions with distinct individual purposes and priorities can realistically share resources on a large scale. The goal of promoting improved resource sharing and evaluating the impact thereof represents a major challenge to BRB staff for the future.

ADMINISTRATIVE ISSUES

New Applications

Opportunities to further respond to the changing priorities through biotechnology are not limited by talent in applicant resources but by fiscal stringencies. This is apparent when only three new resources could be

initiated from a population of 21 applications with outstanding priority scores (100-200).

This population of unfunded applications contained 18 new applications and one supplement. Should this fiscal condition remain where priority scores in the region from 100 to 200 continue to go unfunded, this program area will be unable to attract the high-level talent wishing to contribute to biomedical research through Biotechnology Resources.

Competing Renewal Applications

Because of the length of time (upwards from three years) to bring Biotechnology Resources to optimal operations, emphasis is continuously placed in funding the first competing renewal applications. This is necessary because these resources represent a long-term development of a few comprehensive units of substantial magnitude in staff and in equipment/instrumentation, as opposed to a discipline-oriented research project.

The programmatic problem here also has its foundation in the fiscal stringencies in the grants program. These fiscal constraints permit funding of competing renewals in the upper range (100-200). These renewal applications are generally phased out if their priority score is greater than 200. Most phase-out cases occur because uncontrolled circumstances prevented the resource staff from achieving their potential contribution at the planned rate. Others are phased out because they are unable to keep pace with the technological advances, mainly because new solutions to life science research needs are constantly evolving, and it is difficult for facilities to avoid being locked up in a fixed environment. Additional program resources would permit more flexibility in recovering those resources having potential to meet the new needs of their user community.

As seen from this discussion, the administrative issue raised here is the direction to take in fulfilling the special interest of the biomedical community in utilizing resources. The presence of untapped capability is of concern to the NIH and was one of the major points addressed by a recent DHEW Audit Agency draft report. There will be discrete directions for each type of resource and the promotion responsibilities of each direction will have to be carefully defined in form and function.

Fiscal Year 1972
Annual Report
Chemical/Biological Information-Handling Program
Division of Research Resources

Introduction

The Chemical/Biological Information-Handling (CBIH) Program has sought to define, establish, and introduce into effective usage a computer resource for both personalized and collaborative data management and analysis supporting the research needs of pharmacologists and medicinal chemists. The conviction underlying the establishment and activities of the Program is that such a resource, drawing on the most advanced methods of information science and technology, can be an immensely valuable logistical and cognitive aid to pharmacology investigators. This computer resource can accelerate the acquisition of new pharmacological knowledge by facilitating a formalistic rather than an empirical approach to the study of molecular structure/biological activity relationships. After several years of careful planning and consideration of implementation alternatives, the CBIH Program during Fiscal Year 1972 assembled the working components of an initial version of this pharmacology research resource.

The central component of the resource is an integrated system of computer programs called "PROPHET." PROPHET's capabilities include data management, analysis, and display features which are specially tailored to the forms commonly used by pharmacologists. These features will be refined and extended as collaborating pharmacologist users of the system assess the utility of existing features and their need for additional information support functions. Groups of these pharmacologist users/collaborators commenced exercising PROPHET during the past year.

The CBIH Program also supports basic research and research demonstration efforts which have promise of increasing the future utility of the computer research resource. Present emphases of this sponsored research program are on theory formation in neuropharmacology and on inferential information retrieval using mathematical models of biological systems.

Program Accomplishments in Fiscal Year 1972

Fiscal Year 1972 saw the emergence of a reliably working version of PROPHET being usefully employed by research pharmacologists in their laboratories. Before the beginning of the fiscal year, Program staff and advisors had selected the Digital Equipment Corporation (DEC) PDP-10 Computer as the best hardware available for Program needs. An agreement to obtain a PDP-10 was signed with DEC. After a rigorous competitive procurement review, a contract was signed early in the fiscal year with First Data Corporation (FDC) of Waltham, Massachusetts, to house and operate the computer. FDC has done an excellent job of installing the computer, bringing it into operation, and maintaining reliable computer service with the most up-to-date versions of PROPHET and DEC computer programs.

The CBIH Program's technical assistance contractor has been Bolt Beranek and Newman Inc. (BBN) of Cambridge, Massachusetts. Prior to Fiscal Year 1972, BBN's chief task was to design and implement a version of the PROPHET System that was easy to use, reliable, and basically useful to pharmacologists. They accomplished this task. During the fiscal year, BBN transferred the PROPHET System computer programs from their own computer testing facility to the CBIH Program computer. It was their responsibility to detect and eliminate operational flaws from the version of PROPHET available to computer-naive pharmacologists working on the CBIH Program facility. BBN also had to provide any necessary materials and instruction to acquaint new users with the system and assist them in their ongoing use of it. They performed these tasks well.

The first collaborative effort to integrate the PROPHET System's information-handling tools into the laboratory activities of pharmacology investigators began in February 1972 with the start of regular PROPHET System usage by a group of medicinal chemists at Northeastern University. The research of this group, which is supported in part by the National Cancer Institute, is aimed at developing and evaluating a rapid chemical assay system for identifying potential chemical mutagens, and for testing a wide range of compounds with this method. Northeastern scientists have already found the PROPHET System easy to use and useful in organizing their data and preparing conference papers. They anticipate exploiting PROPHET's capabilities for the kind of data tabulation, perusal, manipulation and interpretation currently otherwise unavailable to them in any convenient form. They also recognize PROPHET's potential as a "publication" and communication vehicle.

A second group of scientists, at the Department of Pharmacology of the University of Pittsburgh Medical School, began use of the PROPHET System within the past fiscal year. The work of members of this group includes the following projects: 1) A study and compilation of the metabolic pathways of commonly used drugs; 2) A study of firing patterns of neuronal populations; and 3) Analysis of the time-independent relationships among biochemical substances with the aid of computer simulation. As a result of their use of the system, they not only developed facility in using the data-management tools, but also gained an appreciation of the potential specific applications of these tools for their research. Furthermore, the Pittsburgh scientists even suggested a considerable number of additional capabilities which they would find useful. One member of the Pittsburgh pharmacology group is particularly interested in the potential of the information-handling tools of PROPHET for providing assistance in experimental design at the interface between theoretical models and laboratory data. CBIH Program staff views this as potentially one of the most exciting uses of the PROPHET resource.

Valuable experience has been gained in just the last several months from actual users of PROPHET. Not only have the personalized information-handling tools of the basic PROPHET service version been subjected to their first rigorous test (and have so far fared extremely well), but the next steps in expanding the capabilities of the system have been delineated.

In Fiscal Year 1972, significant achievement was recorded within the CBIH Program's sponsored research activity. A group of scientists, headed by Dr. Harry Pople, continued their work at the University of Pittsburgh under

CBIH Program sponsorship. Their research over the past few years centered about the use of a mathematical model to embody knowledge about biological systems. They sought to construct a set of computer programs which could assist a scientist in creating a model, and which would help him answer questions about the effects of altering various pharmacological or physiological parameters using advanced heuristic programming techniques. It was their intention that this so-called "executive software" would allow an investigator to ask questions far too complex to be confronted without computer assistance. Furthermore, Pople's group sought to augment the executive software with procedures which could analyze the vast amount of numerical data emanating from a model simulation and give the investigator a simple English-language distillation of the essential results. The investigator would be provided with a simple subset of English with which to create his model, run simulations, and ask questions about the results. The specific system which the Pittsburgh group chose to test its development efforts was a model of the neural control mechanisms governing skeletal muscle movement.

By early in the fiscal year, the Pople group succeeded in creating the desired system of executive software. This system was successfully integrated into operation on the CBIH Program's computer facility. Despite their success, the Pittsburgh workers' experience suggested that the models of neural control described in the literature which had been used in creating their own model simply were not complete enough to be translated into a "sound" operational simulation model. The most important question was now identified to be how and on what (possibly incomplete or inconsistent) models did researchers base their theories. This inspired an effort to design a software system in which: 1) the data and, significantly, the assumptions underlying some version of a neuropharmacological model could be encoded and analyzed; 2) software aids would be available for inferential information retrieval based on the encoding/analysis system; and 3) a program with a hypothesis generation mechanism based on abductive reasoning would be incorporated. This train of developments is intended to arrive at a system of automated model building on a footing much more firmly rooted in literature data and explicit hypotheses.

Prospects for the Program in Fiscal Year 1973

Certainly the major development anticipated within the CBIH Program for Fiscal Year 1973 will be the active collaboration of research pharmacologists and medicinal chemists in the use of PROPHET. One aim of the Program has been to create a basic discipline-oriented data management system into which new capabilities can be integrated as the need for them is recognized. The basic system now exists. As pharmacologists use the system next year in the context of their laboratory activities, they will perceive new needs and will guide the further elaboration of PROPHET accordingly. Hence, we anticipate growth in the system in ways not known at the present. We hope to learn more about how pharmacology researchers use information in their own activities, particularly in the experimental design phase. We also hope to identify those information-handling tools which will be most helpful in facilitating collaborative research and exchange of results. Thus, PROPHET can play two roles in the research process: first, it can fulfill its primary task as a logistical

and cognitive aid; and second, it can help the CBIH Program characterize the needs and methods of the research community.

One of BBN's tasks over the last eighteen months has been the design of a system to enable scientists to create and exercise mathematical models, with full access to the other data management features of PROPHET. The preliminary design is completed. In Fiscal Year 1973, BBN will collaborate with pharmacologist users of PROPHET to determine how well the specifications for the mathematical modelling "package" meet the actual modelling needs of researchers. Based upon this determination, decisions about the future direction and scope of efforts to implement a package of modelling tools within PROPHET will be made.

Basic research conducted by the workers at the University of Pittsburgh will continue in Fiscal Year 1973. The emphasis will be in the area of theory formation in neuropharmacology. As indicated above, this area has been identified as one of key importance for insuring that the use of advanced analytical methods of information science is on a secure theoretical and empirical basis. The Pittsburgh project has great potential for providing unique and extremely powerful pharmacologically oriented information processing tools in the next few years. The CBIH Program staff views this as a future option in the continual development of the central PROPHET System. It is precisely for this reason that the continuation of projects such as this one is considered vital to the usefulness of the PROPHET System to pharmacology for years to come.

Administrative Considerations

The best measure of success for the CBIH Program will be whether investigators supported by the various categorical components of NIH eagerly seek to use PROPHET and are willing to devote some of their intellectual and fiscal resources to the exploitation of that tool. During Fiscal Year 1973, CBIH Program staff hopes to refine the mechanism for identifying and introducing new user groups onto the system. The intent at the present is to add one new user group every two to three months for an indefinite period. Allocation of costs between the CBIH Program and other funding sources follows a set of policies approved by the Assistant Director for Collaborative Research, NIH, in January 1972.

Limitations of fiscal resources have forced the Program to undertake various technical developments in a sequential order when it would be highly desirable to undertake them simultaneously. It has been necessary to delay the development of information-handling capabilities directly aimed at promoting collaborative research and the accretion of public files. The same has been true of tools of a more analytic and prospective nature than the basic file manipulation and retrieval tools receiving first attention.

Equally serious has been the constraint imposed on the research and development component of the Program. For the FY 1973-78 period, the tentatively established level of $1 million per year would be marginally adequate at best to maintain the viability of the PROPHET System. This funding level would

provide absolutely no opportunity for the kind of forward looking research and development efforts on which a pioneering technological effort like PROPHET must continually depend. Additional funding increments will be necessary to preserve our development options in the future. They will be necessary to insure that the information-handling tools of PROPHET will adapt the best and most advanced results of computer science to grow in a way that remains responsive to the growing and changing needs of the research community it serves.

Fiscal Year 1972
Annual Report
General Clinical Research Centers Branch
Division of Research Resources

Clinical research is essential if human diseases and conditions are to be studied scientifically when suitable nonhuman models do not exist for studies in vitro or in vivo. Even when suitable animals are available, it is usually necessary to extend such research studies to human subjects, prior to the final application of new modalities for prevention, therapy or management of human disease. The fundamental study of human physiology, with its broad implications for the maintenance and restoration of health, requires the utilization of human subjects. Progress and productivity in clinical research depends heavily on proper resources support including the capability to provide the specialized environment necessary for such patients. The General Clinical Research Centers provide such a national resource. Since these centers are multicategorical, research conducted therein benefits from the interaction of investigators who share experience and expertise from a variety of clinical research interests in the design, conduct, and interpretation of their investigators. Traditionally, support has been provided for a fixed number of hospital beds in a discrete area chiefly within university-affiliated hospitals staffed by specialized nursing, dietary, and laboratory personnel.

Although most of the "general" centers can accommodate both adults and children, approximately 21 percent of the supported centers focus on pediatric problems and a few have been built around premature infants, maternal-child, and acute surgical research problems. These institutional resources are available to all qualified investigators within the parent institution for use in studying patients admitted as part of approved research projects.

The objectives of the General Clinical Research Centers Program are: (1) to provide facilities and personnel sufficient to establish throughout the Nation, the optimal environment for human clinical investigation; (2) to promote the rapid application of laboratory and basic science research advances to the immediate care of the clinically diseased individual; (3) to increase the total body of knowledge of the etiology, natural history, therapy and prevention of human disease; (4) to promote the improvement of standards of medical care within grantee institutions by functioning as a model of medical excellence; (5) to train physicians, medical students, nursing personnel, dietary personnel, and paramedical personnel in the techniques and disciplines of clinical investigation; (6) to contribute to the maintenance of a national core of full-time faculty investigators and clinical educators through the support of physicians and other trained scientists in center professional categories; (7) to provide a resource for the hospitalization of patients being studied by investigators whose basic research is supported by peer group reviewed Federal grants; (8) to encourage and support the development and practical application of new laboratory

diagnostic techniques through the sophisticated utilization of core laboratories; and (9) to promote the development of more efficient therapeutic diets and more carefully analyzed research diets through the independent research activities by program-supported personnel.

During 1972, the program supported 84 discrete inpatients centers from the pool of applications. Although centers currently exist in roughly two-thirds of the teaching medical institutions, a number of institutions with great potential for scientific excellence do not yet have centers.

Over the past two years, over half of the centers have been reviewed on site, and detailed analyses have been made of a number of the components common to all centers within the program. From this body of information, a number of mechanisms by which the program may be further improved have been initiated or are now under active discussion. For example, prior to the current year support has been provided for a fixed number of hospital beds in a discrete geographical location staffed by specialized nursing, dietary, and laboratory personnel. The original concept of a center as a physically discrete inpatient unit has evolved over the years in response to the changing needs of the Nation's clinical investigators. The concept is now being extended beyond the research limitations of a solely inpatient unit to include facilities and personnel necessary to incorporate an outpatient or ambulatory clinical research program. Thus, 25,000 outpatient visits were supported during the past year. The last phase of the plans for outpatient studies, that of providing geographically separate outpatient facilities is now active with one such center anticipating 5,000-10,000 outpatients visits per year. A second proposal for a geographically discrete outpatient facility is currently under review. The additional latitude provided by this program extension represents an important complement to inpatient studies.

The GCRC Program grew at an almost constant rate between 1960 and 1967. In the past few years, rising costs and fiscal restraints have prevented expansion and have forced support for fewer centers and a decreasing number of beds. Table I depicts this program history.

Table I. GCRC Program, FY 1960 - 1972

Fiscal Year	Institutions with GCRCs	Medical Schools with GCRCs	GCRCs Awarded	Funded Beds	Apportionment in millions of $
1960	8	8	8	-	3
1961	31	30	32	142	8
1962	50	46	56	404	27
1963	59	51	66	566	30.9
1964	66	56	77	758	27.1
1965	70	58	82	891	26.9
1966	74	61	88	998	28.5
1967	75	62	91	1,056	28.5
1968	75	62	91	1,051	30.4
1969	77	64	93	1,023	35.0
1970	77	64	93[1/]	904	35.0
1971	72	56	82	881	38.0
1972	74	58	84	907	42.2

1/ In 1970, fiscal constraints necessitated a phase out budget to 11 centers and two children's centers were amalgamated with an adult center at the same institution.

The program has been able to operate in the face of sharp inflationary rises and modest budget increases for several reasons, such as the closing of 10 centers in 1970, the reduced number of beds supported, the savings realized through new discrete costing procedures, service patient policy, and studies being done on an outpatient basis rather than an inpatient basis. Despite budgetary constraints in recent years, the program continues to support the best available resources for clinical research. Two-thirds of all hospital beds in the Nation specialized for research on human subjects are supported by this program. The number of scientific papers published each year has continued at a relatively stable level despite severe reductions in awards to each center in the past few years. The total output of original scientific articles since 1967 is shown in Table II.

Table II. Center Publications

Year	No. of Publications
1967	1,477
1968	1,982
1969	2,068
1970	2,315
1971	2,201*

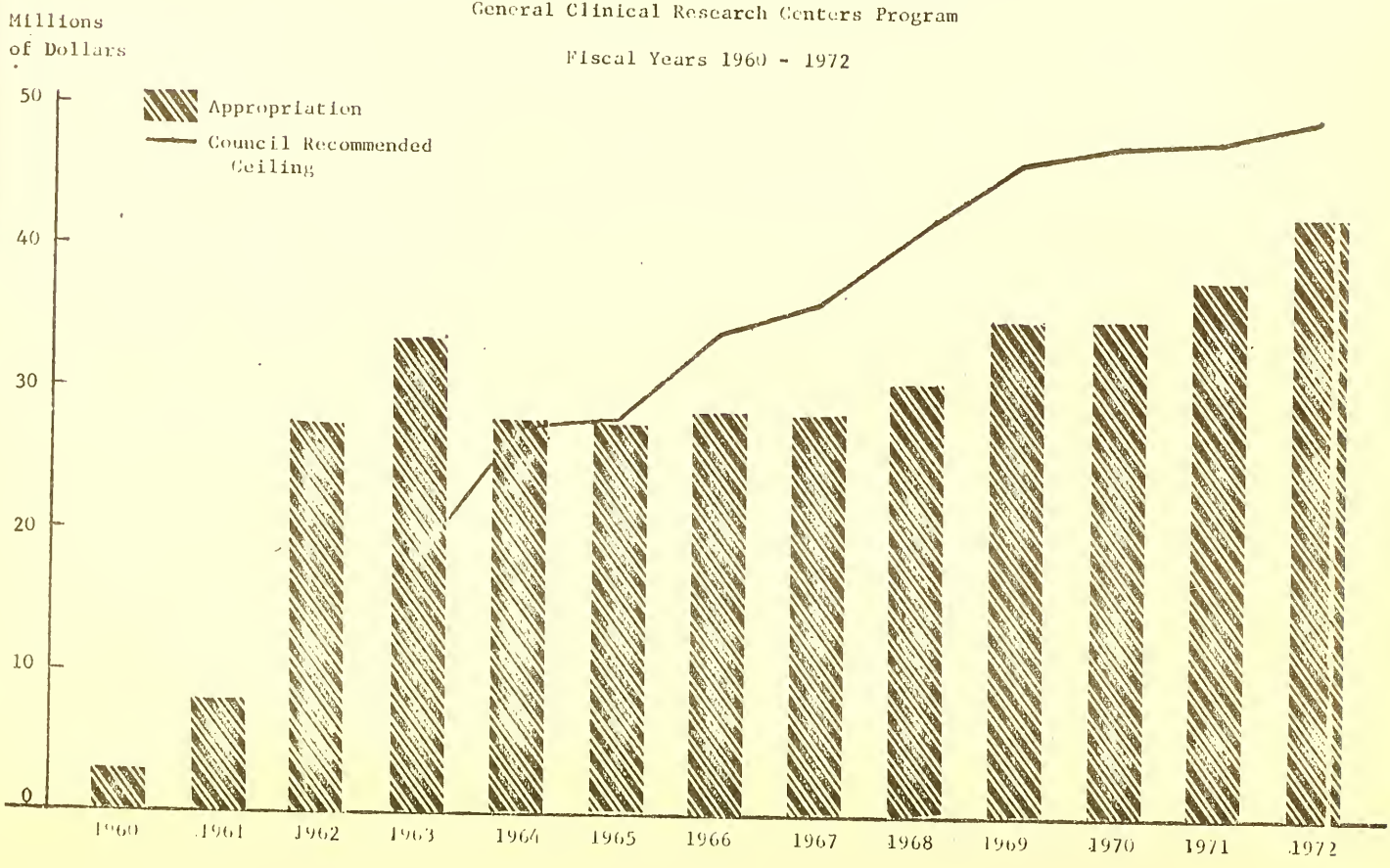
*includes 101 publications involving outpatients

Figure 1

General Clinical Research Centers

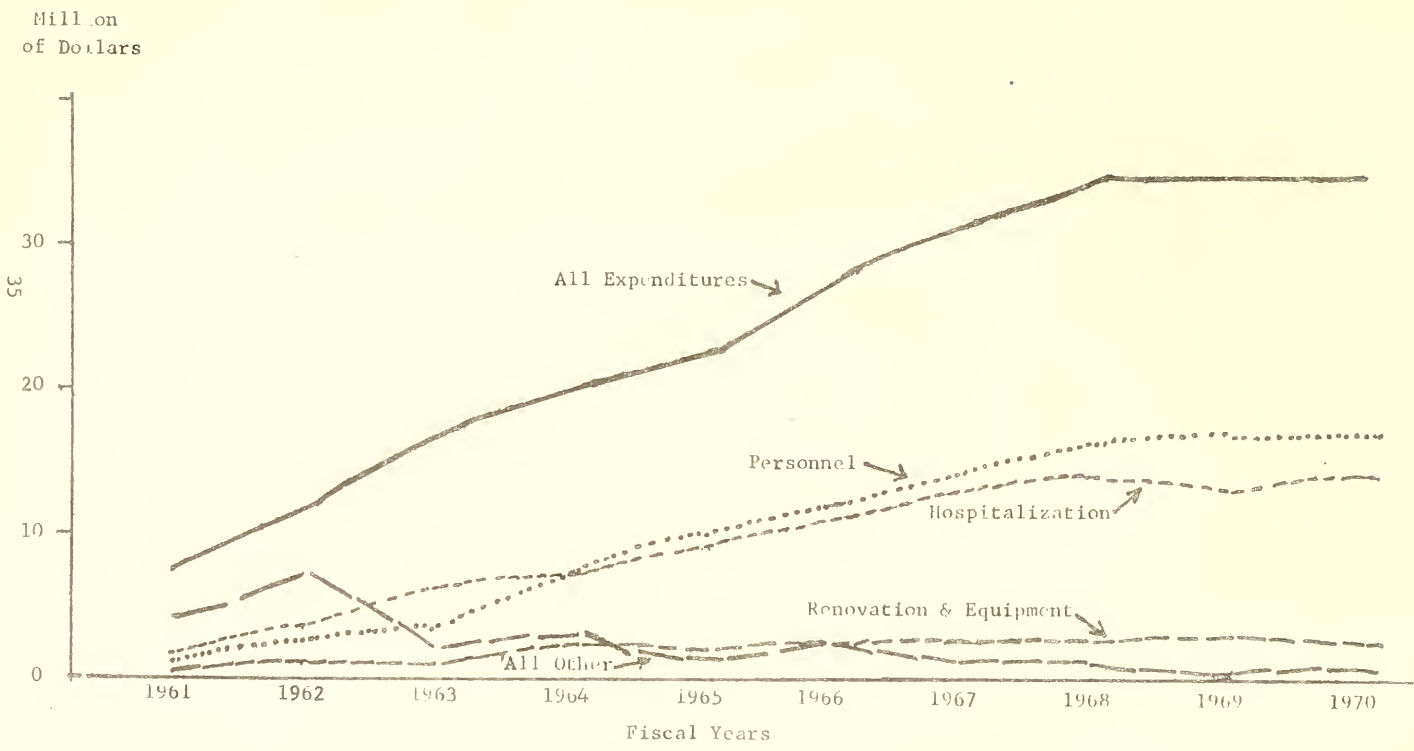
History of Appropriations and Ceilings Recommended by the
National Advisory Research Resources Council for the
General Clinical Research Centers Program

Fiscal Years 1960 - 1972



History of Expenditures Under the General Clinical Research Centers Program,
by Selected Budget Categories

Fiscal Years 1961 - 1970*



* Fiscal Year 1970 includes the Amount Awarded data for all ROE's (9) not yet received.

II. Training

Within the centers, senior scientists, research fellows, and house staff are exposed to increasingly sophisticated methods and concepts of clinical research. Such training is essential for continued development of competent investigators and for improved medical care in the Nation. In these centers, future medical practitioners develop foundations of knowledge that facilitate critical evaluation of new medical discoveries with which they will be confronted in the course of their careers. In addition, the centers assist in the training of large numbers of paramedical personnel. They are the primary hospital facility in which nurses, dietitians, and laboratory technicians gain practical experience in newly developed patient care techniques, generally resulting in better quality of hospital care. Table III shows the numbers of individuals receiving training in clinical centers in the past eight years.

Table III. Training in GCRCs

Fiscal Year	Medical Students	Interns	Residents	Fellows	Totals
1964	582	288	568	579	2017
1965	1,060	362	937	791	3150
1966	1,684	609	1,261	1,190	4744
1967	2,178	682	1,398	1,104	5362
1968	2,538	863	1,576	1,227	6204
1969	2,937	1,019	1,852	1,325	7133
1970	2,614	912	1,707	1,331	6564
1971	2,852	868	1,514	1,215	6449

III. Fiscal Summary

Figure I provides, in graphic form, the history of program appropriations and program ceilings recommended by NARRC (National Advisory Research Resources Council). After an initial period of six years where appropriations were more than adequate to meet expenditures recommended by the NARRC, the following years have seen appropriations falling far short of Council recommendations.

Figure II gives a history of expenditures over the years. It is obvious that personnel and hospitalization costs have been the key factors in the rising costs of the program. Because the number of active beds supported have been forced into a steady decline, personnel and hospitalization costs have stabilized since 1968.

V. Special Program Projects

A. Public Information

1. Television Documentary

During the past winter, program staff has again cooperated with Alan Landsburg Productions and the Information Office, DRR, in the development of a second hour-long television documentary entitled "Life, Death, and the American Woman." For several months, teams of cameramen filmed the lives of several American women selected to be representative of situations which are jeopardizing the Nation's health. The documentary dramatized the fashion in which the life-styles of American women were undermining their health, and how medical science could improve their morbidity and mortality. Physicians associated with GCRCs played a prominent role in the documentary and were shown facilitating the care of these women.

In this dramatic fashion, information was presented to the American people as to how life-style is endangering the health of large numbers of American women and positive information was presented relating to how these life-styles may be altered to promote better health. Through the agency of this television documentary, the GCRC Branch staff feels strongly that it is making a direct contribution to improving the health of the American people. Also, the television program served to highlight many other contributions of the GCRC program.

2. Publication on Clinical Research Advances in Child Growth and Development

A second public service activity which the Branch has undertaken has been the preparation of a booklet "How Children Grow - Clinical Research Advances in Human Growth and Development." This booklet, designed for the intelligent layman, but of sufficient sophistication to be useful to medical students and to the nonspecialist physician, undertakes to review new clinical research findings which have been derived from research in child growth and development within the past several years. The majority of the work detailed within the booklet has resulted from efforts on GCRCs; however, clinical research results from efforts other than on these centers have been included and given prominence consistent with their importance. The booklet, when published in late summer of 1972, should serve again to underline the importance of clinical research in one circumscribed area and to demonstrate the degree to which work supported by the GCRC program is involved in that effort.

B. GCRC Program Evaluation

GCRC grants were awarded first in FY 1960. Activities of the centers have been monitored by staff, center programs have been reviewed periodically by consultants (principally through the GCRC Advisory Committee and the NARRC), and staff has conducted studies of (1) specific operational components such as core laboratories, dietary activities, bed support systems, and space usage charges, and (2) certain scientific areas of investigation such as

human transplantation and inherited metabolic diseases. GCRCs have not been evaluated systematically in a manner that measures (1) the degree to which GCRC program objectives are being met, (2) the quantity and quality of research output of the centers, and (3) the impact of the program on the biomedical research community, medical education and training, and health care. The accrued experience among the centers warrants an evaluation, in terms of these factors, and to determine whether new objectives should be sought through program modification.

The GCRC Branch has developed an over-all scheme to conduct such an in-depth evaluation. The scheme has the following three phases and related input:

Phase 1. Review and clarification of program objectives and execution of appropriate study techniques to determine whether or not these objectives are being met. These studies will also provide important data for assessment of program impact.

Phase 2. Evaluation of specific components of the resource, i.e., core laboratory, diet kitchen, outpatient program, etc.

Phase 3. Review of data obtained in Phase 1 and Phase 2 to determine: (1) the need for changing the objectives, (2) mechanisms for program modification, and (3) the need and recommendations for continuing evaluation.

A subcommittee of the GCRC Advisory Committee has been participating in both the development and the execution of the evaluation plan. Qualified ad hoc consultants have agreed to prepare contribution papers which will be designed to document the contributions that the GCRCs have made to the advancement of research knowledge in specific human disease areas. Contribution papers are contemplated in the following areas: diabetes, growth and development, and serum lipid disorders. In addition, a start has been made to develop research profiles of the aggregate and individual GCRCs. In 1971, information on every project conducted on GCRCs for the grant period October 1, 1969, through September 30, 1970, was obtained. This information includes the project title, an anatomic-pathological code assigned by the investigator, the name of the investigator(s) conducting the project, the number of discharged patients and discharged patient days. The data also includes NIH, other Federal and nonfederal grant support. All NIH grants were verified against Division of Research Grants records. The data captured will enable staff to determine the spectrum of research conducted in GCRC resources. In addition, information concerning the number of projects conducted in various research fields will be compiled. The cost per patient day in each center is also being included in the data so that corresponding dollar figures will be available for protocols in specific areas. At present, the same information for the grant year ending September 30, 1971, is being readied for input into the system. When this data capture is completed, comparisons between the two years will disclose trends that might assist in making program projections.

C. Industry-Sponsored Drug Research

The GCRC staff has been cooperating with the Drug Research Board, National Academy of Sciences, to see if there is any way that beds in the centers which were closed in 1970 could be used for health-related drug studies sponsored by industry. A recent survey of the 10 centers has disclosed that five of these centers were approached by industry representatives for the conduct of such studies. Of the five centers, one center is being used for industry-sponsored drug studies and a second center is in the final stages of negotiation with excellent prospects for initiation of drug studies in the summer of 1972.

D. Clinical Information (CLINFO) Contracts

The Division of Research Resources (DRR) is the primary component in the NIH extramural programs sponsoring both general clinical research and the advancement of computation and other health-relevant technologies which contribute to clinical research. As such, DRR has a keen interest in the prospect that investigative tools emerging from the physical sciences, mathematics, and engineering might have significant utility in facilitating research on human subjects. Through its nationwide research resources of GCRCs and biotechnology resources, the DRR plans to encourage the development of new tools and adaptation of existing technologies for use in clinical investigation.

The fundamental premise in the program is that no matter how powerful and malleable technology is, adequate tools for clinical investigation will not appear on a regular basis unless clinical investigators are intimately involved throughout the design-development-evaluation spectrum. A decade of experience in biomedical computing has shown that computer systems designed for general hospital management or specific health services functions have little value in the clinical research environment. Clinical investigators must be involved in shaping computers and other technologies to fulfill the highly specialized needs of clinical research before work in GCRC environments will be served and served well.

The program under the acronym "CLINFO" has three distinct but interrelated components:

1. the initiation of a collaborative research effort of Division staff and one or more computer-technical contractor(s) on the specific topic "Automated Patient Record Management for Clinical Research;"
2. the reordering of program priorities in the Biotechnology Resources Branch to place a greater emphasis on contributing to the processes of clinical investigation; and
3. the creation of a class of research project grants covering the development, application, and evaluation of new technologies to subserve research in established GCRCs (see section VII).

The collaborative research listed in item 1 above will be a long-range undertaking, using the contract mechanism and placing major emphasis on the identification and solution of those data management problems common to all or most GCRC settings. DRR staff and extramural consultants have selected three GCRCs to work with one information science group beginning in July 1972.

The two grant components of the program will encourage the pursuit of meritorious ideas arising within the DRR's academic clientele. It is expected that activities will be deliberately limited in scope and duration, and influenced by the environment in which they occur.

Future plans for the program of necessity depend upon its successful inauguration. The program is in its infancy. One of its major components, the authority for awarding research resources project grants in the GCRC program, has not yet been received (see Section VII).

E. Annual Ranking of Centers

A newly devised system of rating centers was implemented for the first time last year. The system provides for a priority ranking of all centers project site visited within the year, and which are in a competing renewal or new application status. The system allows the Branch and the GCRC Advisory Committee to have accurate, extensive, and up-to-date information which may impact on funding decisions. In addition, the system allows an approved but unfunded application to compete in two such competitive ranking cycles which, in effect, has the value that any one particular center which is not funded has a second chance to compete for funds. In such an instance, the center actually is rated (or competes) against a total of about one-half or more of the entire population of grantees or applicants within the program over a two-year span.

The system provides that noncompeting renewal applications are funded first and that the annual ranking system determines the funding order for all the year's competing renewal or new applications.

IV. Program Highlights and Scientific Accomplishments

Investigators have used the centers for the study of virtually all aspects of human disease. The scope and vigor of the supported clinical research is demonstrated below by presenting some scientific highlights, the summaries of which were submitted by individual centers as examples of promising work in progress.

Lipids and Coronary Artery Disease

Investigations of the etiology and diagnosis of arteriosclerotic heart disease and blood vessel disease have been of major importance on a number of Clinical Research Centers. It is a well-known fact that the most constant risk factors for heart attack are two fatty substances in the blood, cholesterol and triglycerides. These two substances are elevated in a number of

diseases of plasma proteins which predispose to the development of hyperlipidemia. Patients with high cholesterol and/or triglycerides in their blood may be at 10 to 20 times the risk of heart attack as the normal population. Investigators working on Clinical Research Centers at Rockefeller University, Massachusetts of Technology, Peter Bent Brigham Hospital University of Cincinnati, University of Tennessee, University of Iowa, and University of Pittsburgh have been systematically studying patients with these disorders. Research in this area is extremely important since blood vessel and heart disease are the major contributors to illness and death in this country.

One of the major problems associated with the evaluation and treatment of individuals with abnormally high cholesterol and/or triglycerides is the lack of understanding of the body's synthesis, metabolism and absorption of these two substances. In the GCRC at Rockefeller University, investigators have developed and improved six ways of measuring cholesterol in man. These methods have allowed them to determine the effects of various therapeutic agents on cholesterol absorption, excretion, and synthesis. They have concluded that diets high in polyunsaturated fatty acids cause cholesterol to enter muscle, adipose, and connective tissues and that clofibrate (a drug used in treatment of hypercholesterolemia) mobilizes cholesterol from these tissues and increases its excretion in the feces.

Current medical knowledge indicates that atherosclerosis is a developmental process, having its roots in early childhood. Therefore, over the past two years one of the major studies carried out on the CRC at Children's Hospital in Pittsburgh has been the study of blood lipid concentrations in children with a variety of pathological conditions such as diabetes mellitus, chronic kidney disease, and liver disease. These studies are leading to the development of norms for the concentration of cholesterol, total lipids, triglycerides, phospholipids, and free fatty acids in blood in children of various ages. In addition, information is being gathered on the relationship between alterations in blood lipid concentration in children and adults, confirming the genetic nature of this relationship in many instances. In addition, it seems probable that surveys of normal school children will detect parents and other siblings at risk for arteriosclerotic disease. This is important because of the potential therapeutic implications of early detection detection for the prevention of heart disease and related problems.

The results of projects such as these have led to dietary and drug recommendations for individuals affected by early incidence of coronary artery and blood vessel disease. It is only through continued investigation of basic metabolic mechanisms that rational approaches to treatment and prevention of these disorders can be accomplished.

Hypertension

Hypertension, or high blood pressure, if untreated or poorly controlled, will lead to progressive vascular damage, which in turn predisposes to cerebral stroke or coronary occlusion. Scientific investigations of this disease process are of extreme importance since close to 20 percent of the population suffers from various forms of high blood pressure. While a majority of patients suffer from hypertension of unknown etiology, the number of recognizable and treatable causes continues to increase. A number of Clinical Research Centers have made significant contributions towards identification of correctable forms of hypertension leading to cure either by specific medication or surgical procedure.

Examination of kidney function and X-ray examination of the arteries of the kidneys have been recognized diagnostic approaches to the identification of narrowed renal arteries that result in the elaboration of a renal enzyme, renin, which may cause blood pressure elevation. The measurement of renin in the peripheral blood and in the blood of the right and left renal veins has added to the ability of doctors to identify abnormal kidneys and more precisely identify the patient who will be cured by repair of the narrowed artery or removal of a kidney long deprived of its normal blood supply.

However, X-ray alone does not clearly identify all the lesions of the kidney that cause hypertension. Selected hypertensive patients without X-ray abnormalities of the renal arteries have been examined at the Clinical Research Center at San Francisco General Hospital where researchers utilize a minor surgical procedure involving passage of a small catheter to the sampling sites of the right and left renal veins. Blood samples are examined for renin concentration and by comparing renin levels, the abnormal kidney can be identified. This technique has permitted investigators to identify a potentially large, unrecognizable group of curable patients. The most dramatic result of this approach was was the preoperative diagnosis of a kidney tumor making large amounts of renin. This was the first preoperative diagnosis of this type of tumor made in this country.

A variety of nonvascular abnormalities causing hypertension, such as unilateral obstruction of a ureter, have also been studied at this center. Unilateral elevation of renin identifies the obstructed kidney, which can then be surgically repaired. In addition, small intrarenal arterial abnormalities have been identified by bilateral renin measurements, eventually leading to surgical repair.

Adrenal gland tumors secreting excessive amounts of aldosterone (a potent salt-retaining, potassium-losing, and hypertension-producing hormone) are a well-established clinical entity. This disease entity was first described on the Clinical Research Center at the University of Michigan. Researchers at this center have developed a new technique for detecting tumors in adrenal glands which may be responsible for producing increased amounts of aldosterone and, thereby, causing elevated blood pressure. Utilizing a radioactively labelled precursor of the adrenal hormone, a map

of radioactivity in the adrenal gland is drawn by a scanner revealing the location of the tumor. The location of the tumor is particularly important to the surgeon since the tumor can be on either side and may be difficult to identify even at the time of operation. This diagnostic technique is particularly valuable since it does not necessitate various surgical diagnostic procedures.

Neuroendocrinology

The pituitary gland is referred to as the body's master gland. It secretes more than nine separate hormones which either affect other endocrine glands or act directly on body tissues. Recently, it has become evident that control of the pituitary gland resides in the adjacent brain tissues in an area called the hypothalamus. It is known that hypothalamic hormones, called releasing factors, control the output of pituitary hormones.

The first hypothalamic hormone to be isolated and synthesized was the thyrotropin-releasing hormone, TRH. TRH controls the pituitary release of thyrotropin which, in turn, regulates the secretion of the thyroid hormone by the thyroid gland. Investigators at a number of Clinical Research Centers, including the University of Southern California, Baylor College of Medicine, Northwestern University, and the University of Alabama, are actively studying this hypothalamic releasing factor in patients with pituitary and thyroid disorders.

Recent medical reports indicate that a small but significant group of previously normal women may experience infertility and absence of menstruation after discontinuing the use of oral contraceptives. The mechanism of the so-called "post-pill amenorrhea" is not totally understood. Studies at Temple University Clinical Research Center have shown that the post-pill suppression of menses appears to be due to a specific suppression of the brain centers responsible for the release of FSH and LH (pituitary hormones that cause the ovary to stimulate growth of an egg and, ultimately, ovulation). An attempt was made to stimulate ovulation and menstruation with a relatively new agent, clomiphene citrate. This drug presumably acts on certain brain centers to cause the release of FSH and LH which, in turn, stimulate ovulation and menstruation. Fifty percent of the treated patients have responded.

Research of this type has greatly increased understanding of the regulatory mechanisms of the human endocrine system. Since so many vital functions are controlled in this area of the brain, the ability to detect any derangements by objective means constitutes a major breakthrough in the ability to understand endocrine function in man. Indeed, a variety of illnesses may find their origins in defective hypothalamic function. Preliminary evidence would indicate that such problems as severe obesity, some menstrual disorders, and certain types of psychiatric illnesses may, in large measure, be reflections of disorder in hypothalamic activity.

Bone Disease

Diseases of skeletal bone constitute a significant cause of disability in the adult and childhood population and create a need for extended and expensive medical care for patients of all ages. Several Clinical Research Centers are actively involved in a search for effective drug treatment and research directed towards increasing the understanding of bone disease and metabolism.

Thyrocalcitonin is a hormone recently isolated from the thyroid gland which has the property of decreasing the rate at which skeletal calcium is resorbed. The efficacy of the hormone in treatment of demineralizing bone disease is being studied in the Clinical Research Center at Downstate Medical Center. The drug has been used effectively in the treatment of various bone diseases, including Paget's disease (a disease which involves rapid destruction of various bones of the body and affects three percent of all persons over 40 years of age), osteogenesis imperfecta (a disease of bone formation in children), as well as the skeletal complications of sickle cell anemia, and bone lesions caused by disseminated malignant tumors.

In the Clinical Research Center at Roswell Park, Buffalo, New York, another type of drug is being used to study and treat bone disease. Mithramycin, a new antibiotic, with the unique property of lowering calcium levels in the blood and slowing bone resorption, is being tested in patients with Paget's disease and patients with osteoporosis, a disease which leads to depletion of bone calcium stores. Osteoporosis may affect as many as 20 percent of the elderly population and is an important factor in contributing to the high incidence of bone fractures in older persons. Studies with this drug indicate that control of symptoms and the biochemical abnormalities of both diseases may be obtained by the use of small doses of mithramycin. Studies conducted at these centers require the metabolic balance conditions, close observations, and sophisticated biochemical studies available in a GCRC environment.

Another interesting aspect of bone disease has been studied at the University of Missouri center. It is known that patients receiving chronic anticonvulsant therapy for seizure disorders have a tremendously increased disposition to a bone disease called osteomalacia, a chronic, debilitating disease characterized by defective calcification of normal bone matrix. The significance of these findings becomes readily apparent when one considers that conservative estimates indicate that fifteen million individuals suffer from epilepsy, and these studies indicate that 25 percent of these patients have biochemical findings consistent with osteomalacia. At the University of Missouri center, they have studied several adult patients who suffer from severe osteomalacia secondary to anticonvulsant therapy. These studies suggest that pretreatment of all epileptics on anticonvulsant therapy with small daily amounts of vitamin D may prevent the crippling consequences of osteomalacia.

Infectious Diseases

Many studies concerning the treatment and understanding of immunological and infectious processes are under way in clinical research centers. At Baylor College of Medicine Clinical Research Center investigators have been raising a child with severe immune deficiency disease in a germ-free environment. Children with this disease invariably die before two years of age; however, by raising the child in this germ-free environment, the investigators are attempting to protect the child in hopes that he will outgrow his disease. At the same time, detailed studies are under way to learn more about his immune system. Such studies will hopefully provide knowledge that will not only help treat the child but increase understanding of the human immunologic system. Among the most serious respiratory tract problems in infants and children are pneumonia and bronchiolitis. The single most important infectious agent producing serious pneumonia and bronchiolitis in infants is a virus called the respiratory syncytial virus (RSV). This viral infection spreads in an epidemic fashion through urban communities each year at slightly different times but usually during the colder months. As a result, there is a large increase in hospitalization of infants and children. The kind of illness produced frequently requires hospitalization with intensive care. Presently, no antibiotic is effective against this infection. Vaccine using "killed" RSV has been developed but thus far is ineffective in preventing infection; in fact, it tends to produce sensitivity which makes natural infection with the virus more severe. Therefore, scientists at the GCRC at Georgetown University have concentrated on developing vaccines from attenuated or weakened RSV. In this center, an RSV adapted to grow at cold temperatures was given to children and infants of gradually decreasing age. Antibodies against RSV were illicited in both serum and local secretions. However, in the very youngest children without prior exposure to viruses, there were symptoms of respiratory tract infection which, although mild, were greater than judged to be acceptable in routine vaccination. Currently, this group of researchers is administering another RSV which grows exclusively at lower temperatures. In the 26 infants and children nine months to six years of age who have received this new vaccine, significant rises in serum and nasal secretion antibodies occurred. No illness occurred in individuals who had prior exposure with RSV and infection in infants without prior RSV resulted in only a mild cold without fever or systemic signs.

Hepatitis

Viral hepatitis is still an important unsolved infectious disease problem in the United States. In the GCRC at the University of Colorado, they are attempting to contact every blood donor whose blood is found to contain the Australian antigen, a substance found in the blood of a significant percentage of individuals with hepatitis. These donors are urged to attend the GCRC outpatient clinic for interview, examination, and chemical tests of liver function. The results of this study to date indicate that among the blood donors at the University of Colorado blood bank, the presence of

Australian antigen in the blood usually indicates underlying liver disease. Only 15 percent of the donors studied have had no discoverable liver disease. The liver disease in the remaining 85 percent has varied in type and severity from clinically inapparent, low-grade, persistent hepatitis through severe, symptomatic, acute hepatitis to the irreversibly scarred livers of patients with chronic hepatitis and postnecrotic cirrhosis. The study is continuing in an attempt to gather data that will help predict the prognosis for individuals whose liver disease is found to lie in each portion of the hepatitis spectrum mentioned above. Intensive research is also being directed at understanding the immunologic reasons why certain individuals may carry the hepatitis virus for months or years without evidence of liver disease, while others develop one or another of the several varieties of liver disease. Efforts are also being made toward development of means by which the hepatitis virus may be eliminated from the blood of chronic carriers, thus decreasing the pool of infectious individuals in the community. Many aspects of the immunologic response to the hepatitis virus are also under study.

The Use of Vitamin B Complex in the Treatment of Skin Fungus Diseases

The observation that a vitamin B preparation, when applied to a household plant infected with a fungus overgrowth, resulted in elimination of the fungus, has lead to the trial of vitamin B complex topically in the treatment of patients with a variety of skin fungus infections. During the past two years, physicians at Children's Hospital of Pittsburgh have been utilizing this approach on several children with a chronic, severe form of skin fungus infection (chronic cutaneous candidiasis). These studies have included clinical observations of the patients during intervals on the CRC as well as on an outpatient basis. In addition, in vitro (test tube) studies were carried on. Clinical studies on patients with a chronic, severe form of skin fungus infection have shown definite clinical improvement without adverse side effects. The test tube studies, incubating the fungus with multiple vitamin B complex as well as individual vitamin B preparations, demonstrate inhibition of fungus growth. This growth offers great hope for a simple, cheap, effective method for treating or controlling a most difficult skin infection. The approach may also have some applications in terms of therapy for the systemic fungus infections as well.

Blood Disease

Sickle cell anemia is a molecular defect of hemoglobin resulting, especially under conditions of low oxygen, in a rapid destruction of red blood cells. Many studies are in progress at the Clinical Research Centers concerning the management of this disease. It is known that sickle cell children lack a properly functioning spleen which results in increased susceptibility to infection. It has been found that intramuscular immunization against bacteria to which these patients are most susceptible might be the most effective means of compensating for this defect. In addition, many studies are under way to evaluate urea therapy for sickle cell disease.

These studies have shown that urea is not as effective in controlling sickle cell crises as had been thought initially, and therefore other forms of therapy need to be pursued. Recently, carbamyl phosphate has been studied as a treatment for this disease. In addition, investigators are pursuing a clinical trial with sodium cyanate, which they have found to be effective in reversing the sickling process.

Leukemia

The mainstays of leukemia treatment are various cell-poisoning drugs. These agents, which kill the rapidly dividing leukemia cell, produce harmful side effects in leukemia patients. The benefits, disadvantages, and optimal schedules of treatment continue to be a major focus of interest of medical researchers who use the GCRCs. One approach at the center at the University of Minnesota is based upon the observation that white blood cells undergo a cyclic variation in their number and this variation is associated with a rise and fall in a "white blood cell stimulating factor" present in the plasma. As the leukemic cells increase in the blood, the "stimulating factor" decreases, and vice versa. Therefore, by removing large amounts of plasma at a time when the white cell count is low, the "stimulating factor is largely removed. This concept is being applied to the treatment of leukemia patients and early results are encouraging. With further experience and research into the nature of this phenomenon, perhaps this technique will prove useful in the therapy of leukemia.

Drug Studies

The understanding of drug metabolism is an important aspect of the Clinical Research Centers' program. The metabolism of marijuana has been extensively evaluated on a number of CRCs. Investigators are attempting to correlate the behavioral effects and the blood levels of this drug and its metabolites. In addition, a new metabolite of marijuana has been discovered which has hitherto been unrecognized. Other studies concerning the absorption and metabolism of this frequently used drug are undergoing further investigation.

In another Clinical Center study, it has been found that one of the major side effects of antibiotic treatment, diarrhea, may be caused by changes in the normal bacterial flora of the gastrointestinal tract. It may, therefore, be possible to incorporate preventive additives in broad spectrum antibiotic preparations or give specific therapy to patients who develop the bothersome diarrhea. Many studies in this area have increased our understanding of drug metabolism. It has been found that it may be possible to use the absorption of riboflavin as an aid to the diagnosis of several diseases, for example, biliary atresia. It has also been found that salicylamide, a form of aspirin treatment, is absorbed, but that virtually none of this medicine gets to the blood stream unchanged and all of the metabolic products are inactive. Coincident with the publication of these studies, the major manufacturer of the compound removed it from the market. Other studies give preliminary evidence that cortisone treatment, a very common mode of

therapy, results in uncertainty with regard to the amount of the active drug actually getting into the blood stream. The active compound, cortisol, may be the only reliable dosage form.

Diabetes Mellitus

Diabetes mellitus is one of the most common diseases affecting our population. Complications from this disease result in accelerated blood vessel disease, leading to early death by heart attack, blindness, severe neurological abnormalities, etc. A number of clinical centers around the country are actively involved in research to determine not only the causes of diabetes but also to develop improved treatment regimens.

Diabetes is generally considered to be a disease of relative or absolute insulin deficiency. Heretofore, it has been impossible to estimate the quantity of circulating insulin in diabetic patients treated with insulin, because the commercial preparations generate antibodies against all insulin in sufficient quantity to interfere with insulin assays. Investigators at the University of Chicago CRC have developed an extremely sensitive assay which permits calculation of insulin secretory patterns even in diabetics receiving exogenous insulin. The active hormone, insulin, is synthesized by the pancreas as a single chain protein, called proinsulin. Proinsulin molecules, prior to secretion from the pancreas, are split into two molecules. One of these molecules is insulin itself, and the other molecule is termed the connecting peptide, or C-peptide, which is secreted along with the insulin. An assay procedure for the C-peptide has been developed at this center.

It is possible to use C-peptide blood levels in diabetics as a means of determining the secretion of insulin by these patients. Using this assay technique, researchers have shown conclusively that drastic fluctuation in blood sugar, along with extreme sensitivity to insulin, may be attributable to an absolute deficiency of insulin production by the body. Presence of insulin secretion as determined by C-peptide secretion in adults with diabetes may explain why certain individuals who acquire diabetes late in life tend to have more stable insulin requirements. The availability of an assay of this type has far-reaching possibilities. For the first time, investigators can study insulin secretion in insulin-requiring diabetics. Correlations between insulin levels and aberrations in carbohydrate, protein, and fat metabolism may now be studied. This research and related research in other General Clinical Research Centers has greatly increased our understanding of the diabetic disease process, and will have profound impact on future treatment of diabetic patients. Researchers at the Peter Bent Brigham center are studying the detailed metabolic responses of normal and prediabetic man. These studies have helped clarify the hormonal and metabolic adjustments in the fasting state. Such studies will help detect the precise hormonal and biochemical abnormalities seen in diabetics and obese patients and hopefully in the future provide a more rational base for management of diabetes and obesity.

Neurology

An important medical advance in the past decade has been the introduction of L-dopa in the treatment of Parkinson's disease. Many studies are under way at GCRCs to determine the most advantageous method for administration of L-dopa; for example, a related compound, alphamethyldopa, when given together with L-dopa, reduces the body's metabolic inactivation of L-dopa.

Studies concerning the biochemistry of catecholamines in emotional disorders are under way which are attempting to determine which drugs are most effective in patients with these disorders. Studies have been initiated with 5-hydroxytryptophan, a precursor of serotonin, in the treatment of narcolepsy, a disease involving an overwhelming and very frequent desire to sleep and the use of this drug for the treatment of severe depression. It is possible that some forms of depression are related to a deficiency of serotonin and researchers are attempting to understand the causes of this deficiency, as well as to treat these patients by increasing levels of serotonin in the brain.

Studies in epilepsy are under way in order to find more effective therapies. Clonazepam is being tested as a possible effective drug for petit mal seizures. Other studies have developed techniques which allow for the rapid and accurate measurement of anticonvulsant drugs in the serum of patients with epilepsy. Such measurements could be of considerable value in the treatment of this disease. Studies concerning the metabolism of dilantin, the most important drug in the control of epilepsy, have found that this drug persists in the body long enough so that it can now be given only once a day with equally good clinical effects.

Gallstones

Gallstones are one of the leading causes of illness in the United States today. It is estimated that 15 to 20 million people harbor gallstones. Some of these stones are composed only of calcium carbonate or of bilirubin (a breakdown product of the blood's hemoglobin), but the vast majority contain cholesterol, either as a major component or in pure form. The only accepted treatment of this potentially debilitating and even fatal disease is surgical removal of the gallbladder--cholecystectomy.

Recently, medical scientists have increasingly focused their attention on the mechanisms of gallstone formation and bile composition. Studies showed that many patients with gallstones have abnormally low amounts of bile acids available for keeping cholesterol in solution. Thus, the idea arose that gallstones may be prevented or, if already present, dissolved by altering the concentration of bile acid in the gallbladder.

A small-scale test of this hypothesis has been carried out on the General Clinical Research Center at the Mayo Clinic. Seven women with cholesterol gallstones were given chenodeoxycholic acid (CDC), a bile acid, for a

period of 6 months to two years. In four of these patients, the gallstones were seen, by means of an X-ray test, either to disappear or to become appreciably smaller in size. The medical researchers who conducted this study are quick to point out that more detailed tests involving larger numbers of patients are necessary before CDC can be used by the practicing physician. However, this study has shown very clearly that the possibility of a safe, effective, nonsurgical treatment of gallstones exists. If CDC proves clinically useful, the benefit to the public in terms of dollars saved and illness and pain relieved will be considerable.

Transplantation

The GCRC Program has played a vital and extensive role in human organ transplantation research. In the past decade, leading investigators in the field of transplantation have made heavy use of the facilities provided by the GCRCs. At the present time, many concepts and techniques developed from studies conducted on GCRCs have been incorporated into beneficial treatment programs for transplantation patients. In particular, progress in kidney transplantation and in the development of artificial kidneys has led to much more widespread and accepted use of these techniques for persons suffering from chronic kidney failure. However, the high prevalence of kidney failure in the United States and the persistence of some deficiencies in our knowledge of the causes and treatment of renal disease have stimulated continued research on GCRCs. For example, the problem of early recognition of rejection of a transplanted kidney and the best method for preventing or delaying overt rejection is being studied on GCRCs. At the GCRC at Baylor College of Medicine, doctors noted that certain changes occurred in the activity of the white blood cells (lymphocyte) several days before the appearance of signs and symptoms of rejection. In this test, peripheral blood is taken and lymphocytes are separated from other blood cells. Since these cells are the primary ones involved in immunologic reactions, they were tested for increased activity by adding a radioactive chemical (thymidine) to the cells. Normal controls, patients before grafting, and patients after grafting with good graft function all showed a similar degree of lymphocyte uptake of the radioactive material. However, in patients experiencing graft rejection, cell uptake of the radioactive material was 10 to 20 times greater and was noted five to ten days prior to clinical signs of rejection. The test may, therefore, predict rejection and allow alteration of treatment prior to the patient's becoming ill. In addition, it may be performed on an outpatient basis and provide a means of preventing repeated hospital admissions which frequently are necessary to evaluate and treat organ rejection.

Studies on various drugs for the treatment of rejection are under way in several GCRCs. The use of steroids, administered in large one-shot doses, is being investigated at the University of Michigan. It is hoped that this treatment program will avoid some of the complications associated with long-term oral steroid therapy, such as obesity, personality changes, and bone demineralization. Scientists at the University of Colorado GCRC are evaluating the use of a powerful antirejection drug, cyclophosphamide, in

kidney transplant patients as well as in patients with liver and heart transplants. For patients awaiting kidney transplants or for patients unsuitable for transplants, the artificial kidney provides a means for disposing of body wastes and maintaining a useful life. This device is widely used in the United States, but the expense and difficulty in using it has led to a serious lag in its application to a larger number of patients. Innovative development in the design and construction of artificial kidneys is being carried out on the GCRC at the University of Utah. Keeping in mind the cost, ease of use, reliability for home treatments, and safety, engineers and physicians have tested a semiautomatic instrument and revised it so that it is suitable for home use. A new partly disposable artificial kidney is also being evaluated on patients. This device appears to be extremely easy to use and is inexpensive.

VI. Future Objectives and Trends

The underlying goal of the program to provide specialized inpatient and outpatient facilities designed for the conduct of excellent clinical research remains unchanged. That this program has filled a deeply felt need within the medical community is documented by the progressive increase in the number of centers applied for and funded during the history of the program. As pointed out earlier, the productivity of the program may be documented quantitatively by the number of papers produced annually by all the centers and quantitatively by the quality of the scientific journals in which they appeared. However, recent analyses of program function coupled with increasing budgetary constraints indicate that there remain a number of mechanisms by which the quality of the science generated by this program may be further improved.

Although centers are currently extent in two-thirds of the teaching medical institutions in the country, a number of institutions with great potential for scientific excellence do not as yet have centers. Among the highest priorities of the program is the funding of high priority applications for new centers. Between one and four additional high priority applications are anticipated to be received by the end of fiscal year 1974. Highest priority will be placed on funding of these centers.

A large need has been documented by program staff for facilities for the conduct of ambulatory clinical research. In recognition of this need, existing centers have been allowed the option of modifying their current facility to enable increasing use of ambulatory patients as research subjects. Forty-three centers have acted on this option, and many others have indicated their interest. The use of center facilities for such research requires some renovation of existing facilities and some redistribution of personnel allocations within the grants. In centers where the demand for ambulatory facilities is substantial, supplemental funding is required to develop a more elaborate facility and nursing staff.

Continued budgetary constraints have required and will continue to require some reduction in the level of support in program activities in all centers.

However, care has been taken and will continue to be taken to insure that within the confines of available funds the program continues to supply the best possible clinical research resource. As the most costly element in most of the center budgets is hospitalization costs, reduction in hospitalization awards will create pressure within an institution to utilize unfunded beds for service activities. This is particularly true in those hospitals where an acute bed shortage exists. In order to circumvent an undesirable shunting of beds from research to service use, the program has established a discrete costing method in which in effect the entire center area is "rented" from the institution at cost and ancillary services for patients admitted to the unit are awarded on a fee-for-service basis. This mechanism has had wide acceptance among Program Directors; however, negotiation of this method of reimbursement has lagged, and another year likely will be required before the impact of this new method can be accurately assessed on a program-wide basis.

VII. Future Programs

The GCRC Program is seeking authority to approve resource-related project grants. These grants would be funded either as supplemental grants to centers or as project grants to individual center personnel who seek support for a specific activity designed to serve as a prototype model for conducting high quality clinical research.

The program will serve as an administrative locus for projects which aim to upgrade clinical research capabilities through development or adaptation of technical or conceptual tools for use in GCRCs. The possible types of projects envisioned for this program might include, for example,

1) Evaluation of an interactive chemical/biological information handling system in a GCRC;
2) Development of a magnetically-controlled microcatheterization research technique for use in blood sampling, vascular opacification, measurement of hydrodynamic pressures and bioelectric potentials, delivery of therapeutic agents, and perfusion of small discrete segments of tissue.
3) Development of a dedicated, economical, multipurpose data storage and retrieval system for use in a GCRC.

The resource-related research project grant is sought to provide the GCRC Branch with an administrative mechanism for orderly comparison and review of resource-related grant applications and for judicious program management and planning. The currently utilized review and funding procedures for GCRC grants do not provide these administrative commodities in handling resource-related grants. A separate grants program will permit the Branch to allocate a segment of the total GCRC budget for resource-related development activities and to judge the effect of these grants on upgrading the research capabilities of GCRCs. It should be noted that, if authority for this grants program is approved, the portion of the total GCRC budget devoted to it will be small, on the order of $250,000 annually.

Fiscal Year 1972
Annual Report
Animal Resources Branch
Division of Research Resources

INTRODUCTION

The overall objective of the Animal Resources Branch is to support activities that provide, or enable biomedical scientists to effectively use animals to develop knowledge for the prevention and control of disease in man. Special attention is given to those animal resource activities that are broadly supportive of the missions of the various NIH components. The Branch objectives are accomplished through a Primate Research Centers Program, a Laboratory Animal Science Program, and Research Contracts.

PRIMATE RESEARCH CENTERS PROGRAM

The Primate Research Centers, established with Federal funds in the early 1960's continue to provide leadership in the rapidly expanding field of biomedical primatology. The Centers, operated by grant funds, provide unique research environments where biomedical research in a number of important areas is being conducted. During this year, numerous contributions were made in the areas of infectious diseases, reproductive biology, degenerative diseases, and neural and behavioral research.

The core support provided by this program permitted the 101 Center core staff scientists to conduct research on 103 Federally supported research grants and contracts totaling $2.6 million. In addition, 334 collaborative scientists from a number of universities, utilized these facilities to conduct part or all of their research projects totaling some $2.2 million. The program provided salary support for 788 employees including 122 doctoral level staff and 666 technical and administrative personnel. The Centers were active in both technical and research training with some 172 graduate students participating in the research activities as part of their theses requirements.

The extensive review of the Program, initiated in 1971, has been completed, and the recommendations of our advisory groups are being implemented. The major recommendations involved a) the development of research missions for each Center in order to assure a balanced program in research areas mapping on national health needs, b) research on primate biology would be supported in each Center to the extent necessary for acquiring baseline data for the scientific program, and the mission of the National Center for Primate Biology would be changed with this Center being considered on the same basis as the other six Centers and c) the program will devote efforts to determining the availability of primates and to establishing breeding colonies in the Centers.

Research missions for each Center have been identified, and staff discussion with the host university administrators have been conducted. The missions, as identified under each Center, are being implemented.

Because of widely expressed concern about possible decimation of populations of wild primates, two primate population surveys have been undertaken. In addition, efforts have been made to expand the breeding programs in each Center.

The missions and the research activities of the Centers are as follows:

Oregon Primate Research Center

The missions of this Center are reproductive biology, cardiovascular and metabolic diseases, and immune diseases. The reproductive biology program, consisting of some 14 investigators with $0.5 million of project grant support is the most comprehensive and outstanding one in the United States in which the nonhuman primate is used as the experimental animal. The following are examples of research at this Center:

1. Sex of Fetus Regulates Pregnancy Hormones

Scientists at this Center have discovered a phenomenon that may have an important bearing on the sexual development of human infants. The placentas of pregnant monkeys produce much more progesterone, a hormone essential for the onset and completion of pregnancy, when the fetus is female. The same female hormone is produced by the ovaries during certain stages of the menstrual cycle. Apparently the remarkable differences in the level of the hormone in the blood of male and female fetuses is necessary for the proper development of maleness and femaleness in the newborn.

2. Diabetes-like Disease in Celebes Apes

The discovery of a condition that resembles human diabetes in the Celebes ape, Macaca nigra, is unique because this is perhaps the only interrelated, closed breeding colony in the world. Approximately 50% of the adults and 75% of the offsprings show some degree of abnormality. The animals have abnormally high blood sugars and abnormal glucose tolerance tests. The more severely diabetic animals secrete very little insulin into the blood or the secretion is delayed; in either case, the concentrations of blood glucose remained higher for long periods of time after the injection of glucose. Some of these animals have exhibited hyperglycemia; hypertriglyceridemia, and hyperprebetalipoproteinemia; all characteristic signs of human diabetes. Since the family relationships within the colony are known, the inheritance of this disease can be studied and the colony can be bred to develop excellent models for the studies of human diabetes.

Washington Primate Research Center

This Center will continue to pursue its original missions, namely, neurophysiology relating to cardiovascular function and the development of an

extensive collaborative research program involving more than 100 scientists working in many areas of biomedical research. The following is an example of the research being conducted at this Center:

Flow Distribution and Pressure of Blood Circulation to the Brain.

One of the problems in understanding and managing strokes is the lack of knowledge of the basic mechanisms that control the amount of blood flowing to the brain and how that blood is distributed. The old view holds that only restricted chemical changes in the brain can produce variation in blood flow, however, newer evidence suggests that the nervous system itself may control pressure and blood flow distribution. Until recently, the techniques for making the critical measurements in the very small blood vessels supplying the delicate neural tissue have been unavailable. Recent techniques have been developed to measure the blood pressure and flow in these microvessels. The brain of the squirrel monkey, Saimiri sciureus, has proven to be uniquely suited for making these measurements. Because of the close relationship of the nervous system of monkey and man, the results of this study should be directly applicable to human problems of stroke and other cerebral-vascular diseases.

California Primate Research Center

This Center was formerly the National Center for Primate Biology and had as its primary mission the study of primate biology and husbandry. The state of the art in primate biology has matured to the point where it was no longer necessary to devote an entire Center to this purpose. As mentioned previously primate biology will be supported to some extent in each Center. The new mission for this Center is being changed to environmental health sciences and research on respiratory diseases. An example of a completed primate biology baseline study is as follows:

Normal Serum Biochemical Values in Nonhuman Primates.

The normal serum biochemical values were established for six species of nonhuman primates including Macaca arctoides, Macaca fasicularis, Macaca radiata, Cercopithecus aethiops, Cercocebus atys and Presbytis entellus. The sera from these species were studied to establish normative baseline values for 23 chemical constituents. The animal population studied were carefully selected to include mature healthy animals. Highly significant differences in the normal ranges were found when different species and when males and females of the same species were compared. These serum biochemistry baselines will permit a more careful evaluation of various research activities in which these species are employed.

Delta Primate Research Center

The primary research missions of the Delta Center are infectious diseases and nutritional diseases, and an example of this research is as follows.

Pyelonephritis Investigations

Pyelonephritis is one of the major diseases leading to renal failure that is either fatal or necessitates kidney transplantation or chronic dialysis on kidney machines. Normal renal function in Old World primates is similar to that of man, and pyelonephritis can be produced in these animals by inoculation of suitable bacteria. The disease in the monkey spontaneously resolves as often happens in humans. These studies are involved with the factors that convert the acute disease to a recurrent and chronic form and may provide new approaches to therapy.

Wisconsin Primate Research Center

The areas of neural and behavioral sciences and reproductive biology are being continued as the missions of this Center, however, research in the new emerging areas of neurophysiology and neuroendocrinology are replacing the more classical behavioral research. Examples of this research effort are as follows:

1. Implantation and Maintenance of Early Pregnancy

The hormones required for implantation of the embryo in the womb have been defined for several non-primate mammals. The hormonal requirements for this key reproductive process in primates, however, have not been elucidated. Recent experiments conducted in this Center clearly indicate that embryo implantation and maintenance of pregnancy in rhesus monkeys can occur in the absence of the hormone estrogen from the ovaries. If the ovaries of monkeys are removed 307 days before implantation, administration of another hormone, progesterone, will permit implantation and maintenance of pregnancy to term with the birth of normal infants. This suggests that agents to counteract progesterone, if administered following conception but prior to implantation, may be of value as fertility control agents in primates and possibly humans. These studies are currently being extended to include the importance of the pituitary gland for embryo implantation and maintenance. Recent data indicates that following removal of the pituitary, progesterone will not maintain pregnancy to term.

2. Behavioral and Biochemical Effects of 6-Hydroxydopamine

Investigations have led researchers to believe that human schizophrenia may result from a deficit in the enzyme dopamine-β-hydroxylase, causing dopamine to accumulate in noradrenergic

(NE) neurons of the brain. It is theorized that the dopamine, upon release from NE nerve endings, metabolized to 6-hydroxy-dopamine, a drug known to destroy NE neurons. The resulting loss of NE neurons was believed to produce emotional deficits as well as deficits in associative processes which characterize schizophrenia. The effects of 6-hydroxydopamine on brain chemistry and behavior is being studied in rhesus monkeys. Measurements of norepinephrine, dopamine, and tyrosine hydroxylase on monkey brains have been done, and drug doses which produce an apparently permanent 50% depletion of NE have been determined. If this work were to produce an animal analogue of either schizophrenia or depression, it would represent a major advance in the ability to study these diseases.

Yerkes Primate Research Center

The research missions of this Center are neurophysiology and neuroanatomy and the study of neoplastic and degenerative diseases. This Center also maintains the largest colony of great apes--chimpanzees, gorillas, and orangutans--available anywhere in the world for biomedical research.

Neural Mechanisms of Sleep and Wakefulness

Experiments have been conducted in primates on the influence of vestibular stimulation on sleep by rotating the monkey at a constant velocity on a specially constructed centrifuge. Movement of the animal on the centrifuge while rotation is in progress causes stimulation of the semi-circular canals of the inner ear which elicits the vestibulo-ocular reflex. Continuous 24-hour recordings of eye movement, EEG, and EMG were taken before, during and following long periods of continuous rotation. Preliminary findings indicate this form of vestibular stimulation causes significant decrease in the stage of sleep known as "deep sleep." The implication of these findings are indicative of some hazards that may be encountered in prolonged manned space missions on rotating platforms.

New England Primate Research Center

This Center supports an extensive collaborative research program involving some 95 investigators from many institutions. In addition, programs in infectious diseases and pathology are conducted by the Center core staff. An example of the collaborative research projects is as follows.

Studies on Aflaxtoxin in Primates

The effects of the mold metabolite, Aflaxtoxin B_1, is being examined in male rhesus monkeys by a group of investigators at the Massachusetts Institute of Technology. Aflaxtoxin B_1,

which is a potent hepatic toxin and carcinogen in several species, contaminates human food supply in many parts of the world and may be responsible for the incidence of hepatocarcinoma in people from these areas. Primates have been shown to be sensitive to the acute toxicity of aflaxtoxins, but the induction of carcinomas have not been demonstrated. Diets deficient in lipotropes increase the sensitivity of rats to aflaxtoxin carcinogenesis, therefore, this deficient diet along with Aflaxtoxin B_1 is being fed to monkeys in order to mimic the conditions under which humans are exposed to aflaxtoxins.

LABORATORY ANIMAL SCIENCES PROGRAM

The objective of the Laboratory Animal Sciences Program is to significantly improve the capability of institutional animal resources to serve medical research and education programs. This mission has been accomplished through grants for support of disease diagnosis and control, research related to improving animal health and care, special animal colonies that are of unusual nature and special value for certain types of research, studies directed to enhancing the usefulness of animal models for research, general improvement of management and accommodations for institutional animal resources, and postdoctoral and special research training. The Program received appropriations of $6,242 million in fiscal year 1972 and provided 78 discrete animal resource projects, 9 training programs, and 12 fellowship awards.

Resource Projects

The program plan developed last year indicated that increased emphasis would be placed on projects that advance animal resources through production of new knowledge or through development of new technology. The diagnostic laboratories are a program element which have contributed in this fashion as well as by undergirding an institution's animal health program. Annual progress reports continue to document examples of disease outbreaks within animal colonies in which the diagnostic service has played a critical role in arriving at a resolution of the problem. An important facet of the diagnostic program has been the elucidation of new laboratory animal models of human disease and discrete research projects growing out of the diagnostic process. The ability to support indepth studies of naturally occurring diseases has provided a mechanism to evaluate problems and develop discrete research grant applications when additional study is indicated. Several of the laboratories indicated that additional grant support was obtained during the current year based on preliminary studies supported by the resource grant. It is hoped that as the laboratory animal programs continue to mature that more qualified individuals will be in a position to develop research projects. An additional strength of the diagnostic program has been its contribution to training in laboratory animal medicine and comparative pathology. Laboratories are currently supported in all of the institutions where Animal Resources Branch training programs are active. An effort will be made in the coming year to characterize in a definitive manner the contribution of this program element through an evaluation study.

There are 16 diagnostic laboratory programs which are currently active. Three new programs were funded this year. A shortage of appropriately trained specialists (veterinary pathologists, microbiologists) appears to be a limiting factor precluding any rapid increase in number of projects of this type. Special attention has been focused on laboratories which have the potential of serving more than one institution. Several laboratories are providing service to sister institutions in the same metropolitan area or are serving a regional area. Increased activity of this type will help conserve resources and help justify more sophisticated laboratory operations.

Animal welfare has developed into a major program area during the current year. The Animal Welfare Act of 1970 (P.L. 91-579) and the policy developed by NIH on "Care and Treatment of Laboratory Animals (June 14, 1971) focused attention on the proper care and humane treatment of laboratory animals. Congress appropriated $1.5 million in FY 1972 specifically for assisting research institutions in upgrading their animal resource programs. The net effect has been a sudden upsurge in the number of requests for assistance to purchase cages and other animal care equipment and for alterations and renovations to improve laboratory animal facilities. In the first Council review after announcing this program, 17 new applications requesting $1.7 million assistance in the 01 year were received. Twelve of these were approved and funded for $1.2 million in FY 1972. This is in contrast to one new project in the institutional improvement area at a level of $102,000 in FY 1971. In the first review period of FY 1973, there are already 17 applications requesting over $1.7 million 01 year funds. It is obvious that a significant number of approved, greatly needed improvement projects will not be funded if FY 1973 funds for this program remain at $1.5 million.

The Animal Resources Branch program also supported several reference centers and information projects. Examples of these are:

1. A simian virus reference laboratory at the Southwest Foundation for Research and Education at San Antonio, Texas. It now has a working repository of over 60 virus reference reagents and reference antiserums. Ongoing activities of the project are designed to give information regarding the immune status of subhuman primates and the possible cause of outbreaks of overt diseases. Institutions throughout the country have taken advantage of this program. Service functions for outside investigators are of two basic types:

a. Screening sera for the presence of antibodies against a battery of simian and human viral antigens; and

b. Attempted isolation and identification of viruses from a variety of specimens from sick or apparently healthy animals.

2. The Registry of Comparative Pathology, located at the AFIP has continued to augment its collection of specimens from primates and other laboratory animals, domestic and wild animals, fish and birds. Material has been made available to others and utilized for the preparation of exhibits, lantern and microscopic slide sets, and as the basis for a number of publications. In addition to publication of a quarterly "Comparative Pathology Bulletin," the Registry has begun publication of an animal model in each issue of the American Journal of Pathology (initiated January 1972). Consultative activities were highlighted by participation in studies involving sea lions found along the Pacific coast. In this investigation, a definitive diagnosis of leptospirosis was made in an epizootic, characterized by high morbidity with low mortality.

3. A "Registry of Genetic Stocks in the United States" for Gallus domesticus was completed and published by the University of Connecticut. This publication includes characteristics and information on the location of

87 specialized lines and strains, and the inheritance, linkage, characterization, and locations of 103 mutant traits. This information should be of considerable value to scientists by enabling them to identify and locate useful avian models for their research.

Other major activities in the program include the support of animal model development projects and establishment of colonies of special research animals which are not generally available because of maintenance and procurement problems. Guidelines for support of projects in both areas have been further defined during the past year.

Characterization and development of animal models which display potential for rather broad biomedical research utility are viewed as appropriate to the interests of the Animal Resources Branch program. Projects of this nature are carefully selected in terms of potential utility, as well as for the group of investigators responsible for the developmental work. Species which demonstrate several unique features of interest usually require a multidisciplinary approach and a rather extensive period of time to obtain maximum information. Examples include the nine-banded armadillo, in which the human leprosy organism has recently been propagated and which may also prove to be a suitable model for studies on syphilis, mutagenicity, and teratogenicity. Another example relates to the development of deer as a model for sickle cell anemia studies at the Portland Zoological Society that has enabled the investigator to secure research support in this area from the National Heart and Lung Institute.

In addition to the more conventional vertebrate animals, increased consideration is being given to appropriate amphibians, marine mammals, and invertebrate animals as candidates for animal model definition and development. A number of these species appear to offer good potential for studies on a diversity of physiological processes. Such species have not been well exploited in the past because of the paucity of information available concerning anatomic, biochemical, and physiological norms, as well as husbandry and maintenance requirements in captivity. A staff analysis of the use of such animals in biomedical research is currently underway, with a viewpoint toward a modest beginning in this area during the next fiscal year.

Fifteen resource colonies of well-defined animals which possess unique or special characteristics for use in a variety of biomedical research areas are currently supported. These colonies undergirded 76 NIH research projects (total funding level of $5,253,000) and 102 biomedical research projects which derive support from other sources (total funding level of $1,422,000). Examples of these special colonies include wild arctic rodents at the University of Alaska; inbred and mutant strains of rabbits at Jackson Laboratory; squirrel monkeys used in atherosclerosis studies at Bowman Gray School of Medicine; frog resources at the University of Michigan and Louisiana State University; inbred strains of mice at Kansas State University; and hemophilic beagle dogs at Oklahoma State University.

The ARB program has continued to provide core support for institutional primate resources. In accordance with program policy relating to initial establishment and support of such resources for a finite period, several of the well-established resources are currently being phased out. The seven projects in this area which were supported during the past year have undergirded 108 NIH-funded research projects (accumulated funding level of $6,212,000) and 92 biomedical research projects supported by other sources (accumulated funding level of $1,890,000). These research projects include investigations in the areas of reproductive physiology and fetal development, atherosclerosis, hepatitis, organ transplantation, experimental epilepsy, glaucoma and chronic alcoholism.

Training Grants

Training grants are awarded to academic institutions to provide postdoctoral training in laboratory animal medicine. The training is intended to prepare individuals to provide professional care of the many species of laboratory animals, to manage central animal resources, and to give special assistance to investigators through superior knowledge of laboratory animal biology and understanding of research methods. In addition, the trainees are prepared to participate in the teaching of graduate students and young investigators and to pursue their own research interests either as independent investigators or as a member of a research team. Twenty-six trainees are currently enrolled in nine training programs. The usual training period is two to three years.

This year a new guide for preparation of the annual progress report of the individual training programs was developed and distributed. It is anticipated that employment of this guide will facilitate retrieval of information concerning the programs and trainees. Currently available figures indicate that 56 trainees have completed training since the inception of training grants in laboratory animal medicine. Thirty-two of these are employed by medical schools and 18 by other academic, research, or governmental organizations. The majority (33) are functioning as directors or staff members of a vivarium, 20 are engaged in research or are obtaining additional training, and three are engaged in public health and other activities. Although the number of graduates is relatively small, they have filled vitally needed leadership roles in the field of laboratory animal medicine.

Funds to support training have remained at the current level ($352,000) over the past several years. This has placed an increasing strain on the active programs and has resulted in a decreased number of trainees. One of the nine current programs is in the process of being phased out (support will be provided in FY 73 to allow two trainees to complete program). In spite of this action nearly $600,000 would be needed to support the remaining active programs at their Council approved ceilings.

Fellowship Awards

The laboratory animal science fellowship program is being supported by an appropriation of $126,000 for fiscal year 1972. Twelve fellows are being funded during fiscal year 1972. This fellowship program includes both postdoctoral and special fellowships available to qualified individuals who hold the D.V.M., M.D., Ph.D., or similar degrees. Candidates can engage in indepth studies in a discipline or specialty such as surgery, anesthesiology, pathology, virology, nutrition, or immunology through which they can contribute to research animal resources. This program is designed to produce the highly specialized person who can make significant contributions to knowledge regarding laboratory animals.

RESEARCH CONTRACTS

The Animal Resources Branch has used the research contract mechanism as an adjunct to its resource grant programs to support specific, essential services or to initiate activity in vital resource areas that have not responded or are not eligible to respond to the grant mechanism. Although research contract funds for ARB were $760,000 for FY 72, $500,000 of this was specifically designated by Congress to maintain operation of the Holloman primate facility.

The remaining, limited funds were used to continue three contracts and initiate one new contract that contribute significantly to the advancement of laboratory animal science.

Partial Support for the Institute of Laboratory Animal Resources

The Institute of Laboratory Animal Resources (ILAR) is a subsidiary of the National Academy of Sciences, established as a coordinating agency to disseminate information, survey existing and required animal resources, establish standards and promote education in the field of laboratory animal science. Since July 1953, ILAR has received financial support from NIH. These activities are a valuable adjunct to the Animal Resources Branch program. The ILAR meets ARB needs for writing standards and guidelines for animal facilities and care, furnishing information on sources and users of laboratory animals, and providing survey information on the status of animal resources. Special activities include an information service on the sources and availability of over 450 animal models and genetic stocks and a field survey on the abundance and distribution of primates of biomedical interest in selected areas in South America.

Development of a Training Program for Entry Level Animal Care Technicians

This program, developed at the University of California, San Francisco, is specifically designated to instruct entry level animal technicians who are recruited from the socio-economically disadvantaged. Traditional programs have failed to identify minimal skills required for acceptable performance, to properly motivate, and to train this group. Programmed learning techniques are being developed; guidance for instructors and supervisors and identification of the level of skill and knowledge required for acceptable performance as a journeyman animal technician will also be developed.

Environmental Requirements for Laboratory Animals

The general aim of this project at Kansas State University is to determine ventilation and air conditioning requirements necessary to maintain optimal conditions for laboratory animals with respect to temperature, humidity, odor, gases, particulate matter, and microbial content of the air. Definition of these requirements for laboratory animals may provide considerable savings in construction and operating costs in the programs supported by NIH. Prior to the initiation of the project, there was almost no scientific data on these requirements in laboratory animals. Findings to

date indicate that heat produced by caged dogs is two to three times as great as the standard metabolic rate. The project has also shown that ammonia levels in cages can be reduced by the use of certain types of bedding to 1/5 the level present if no bedding is used.

Domestic, Commercial Primate Production

ARB has initiated a new contract with Charles River Breeding Laboratories to provide partial support in determining the feasibility of domestic production of free ranging rhesus monkeys on an island in the Florida Keys. Although the need for this type of program has been long accepted, the low cost of imported wild-trapped monkeys, and long-term investment in a breeding program has discouraged commercial firms from developing this concept. NIH support has stimulated interest in this area. If this program is successful and significant numbers of primates are produced in this country, it will eliminate the many disadvantages in the use of wild caught primates. These include hazards to human health, variability and political uncertainty of supply, and depletion of wild species.

Holloman Primate Facility

This contract is to provide basic support for a large chimpanzee colony and other primates formerly supported by the Air Force at Holloman Air Force Base, New Mexico. These primate colonies will be used as a resource for biomedical research activities oriented towards environmental health and toxicology.

PROGRAM TABLES

Table 1 - Primate Research Centers Program Applications, FY 1972

Type	Number Received	Amount Requested	Number Approved	Amount Approved	Number Funded	Amount Funded
New	-	--	-	--	-	--
Renewal	6	11,128,415	6	9,180,088	6	9,339,024
Supplemental	-	--	-	--	-	--
Continuation	1	1,739,051	1	1,472,976	1	1,767,976
Totals	7	12,867,466*	7	10,653,064*	7	11,107,000**

*Direct Costs Only
**Includes Indirect Costs

Table 2 - Laboratory Animal Sciences Program, FY 1972, Resource Project Applications

Type	Number Received	Amount Requested	Number Approved	Amount Approved	Number Funded	Amount Funded
New	33	2,666,041	23	1,701,842	26[1/]	2,394,487
Renewal	12	779,780	12	624,404	11	723,533
Supplemental	7	161,419	7	71,047	7	85,399
Continuation	41	4,595,099	41	2,876,535	41	3,026,561
Totals	93	8,202,339[2/]	83	5,273,828[2/]	85	6,230,000[3/]

1/ Includes 6 from prior years
2/ Direct Costs Only
3/ Includes Indirect Costs

Table 3 - Training Grant Applications in Laboratory Animal Medicine, FY 1972

Type	Number Received	Amount Requested	Number Approved	Amount Approved	Number Funded	Amount Funded
New	-	--	-	--	-	--
Renewal	4	222,704	3	188,586	3	163,600
Supplemental	1	2,115	1	2,115	1	2,115
Continuation	5	459,160	5	355,827	5	186,285
Totals	10	683,079*	9	546,528*	9	352,000**

*Direct Costs Only
**Includes Indirect Costs

Table 4 - Fellowship Applications in Laboratory Animal Science, FY 1972

Type	Number Received	Number Approved	Number Funded	Amount Funded
New	6	5	5	34,000
Renewal	1	1	1	12,000
Continuation	6	6	6	80,000
Totals	13	12	12	126,000

Table 5 - Laboratory Animal Sciences Program Resource and Research Grants, Project Distribution, FY 1971 and FY 1972

Project Type	1971 Number of Projects	1971 Amount in $1,000's	1972 Number of Projects	1972 Amount in $1,000's
Basic Improvement (Animal Welfare)	14	673	23	2,181
Special Colonies and Models	21	1,342	21	1,250
Primate Resources	9	805	7	879
Resource Research	4	402	7	473
Diagnostic Laboratories	15	984	16	1,162
Reference and Information Centers	6	268	5	297
Totals	67	4,474	78	6,242

Table 6 - Laboratory Animal Sciences Program, Research Utilization of Selected Animal Resource Colonies - FY 1972

No. Colonies	Number NIH Grants	Dollar Value NIH Projects in $1,000's	Number Other Projects	Dollar Value Other Projects in $1,000's
Primate Resources 7	108	6,212	92	1,890
Other Special Colonies 15	76	5,253	102	1,422
Total 22	184	11,465	194	3,312

Total Resource Colonies - 22
Total Research Projects - 378
Total Funding of Research Projects Using Resource Colonies - $14,777,000

ADMINISTRATION

Major administrative activities of the Animal Resources Branch in fiscal year 1972 were: 1) drawing up guidelines for a new program to assist institutions to meet the requirements of the Animal Welfare Act of 1970; 2) assisting in development of NIH and DHEW policy on the care and treatment of laboratory animals; 3) implementing program plans formulated in fiscal year 1971; and 4) developing position papers for OD:NIH consideration regarding support of animal care costs.

In drawing up guidelines for the new program to assist institutions to comply with the Animal Welfare Act, we decided that the major criteria for review should be the overall quality of an institution's plan to improve its animal resource, including administrative and scientific considerations, and the need for animal resource improvement judged in relationship to the institution's medical research program. Furthermore, we decided that animal resource improvement should be approached on an institutional, not a departmental basis. An information for applicants booklet was prepared for the new program. Thus far, 900 booklets have been distributed, including 390 in response to written requests from institutions for information on the animal resource improvement program.

Late in fiscal year 1971, NIH issued a policy requiring that its grantees and contractees assure the NIH that they are evaluating their animal care programs using the standards in the "Guide for Laboratory Animal Facilities and Care" (PHS Publication Number 1024). This policy is administered by the Institutional Relations Branch of the Division of Research Grants, but ARB is called upon for technical assistance. Currently we are serving on a committee to modify the policy and make it applicable to all of DHEW.

Program plans formulated late in 1971 have been implemented. A series of meetings with individual Primate Center Directors and Principal Invesitgators and a joint meeting of Center Directors and Principal Investigators were held to convey our position that each Center should build programs of excellence around one or two major scientific themes in important biomedical research areas. This position was accepted whole heartedly by the Centers.

Program plans in the Laboratory Animal Sciences area to emphasize those projects that advance animal resources through production of new knowledge or through development of new technology have been implemented. Through selective programing and award of grants, our dollar investment in resource-related research and diagnostic laboratories has increased by 18% in each area. Conversely, our investment in special colonies has decreased by 7%.

Throughout fiscal year 1972, we became increasingly aware that animal resources in many institutions were in financial difficulty. As a result, we had conversations with OD:NIH and developed a position paper affirming that it was NIH policy to pay the full costs for animals used in its research projects. We have recommended to the OD:NIH that this position paper be distributed to NIH reviewers, staff, and grantees. This effort is still underway.

A problem of increasing concern is our personnel situation. During fiscal year 1972, our staff decreased from 11 to 10 people, and the average grade of our civil service employees decreased from 7.5 to 6.8. This staff plans and manages 5 programs (Primate Centers, Laboratory Animal Sciences, Training, Fellowships, and Research Contracts); conducts its own reviews through two initial review groups (the number of reviews increased from 52 in 1971 to 79 in 1972); and awards and administers grants and contracts (111 projects in 1972 compared to 98 in 1971). Through dedication and ability the present staff has accomplished its tasks; however, on occasion the work is not accomplished in as timely a manner as desirable. For example, we are not able to complete all site visit reports for mailing to committee members two weeks prior to meetings. Furthermore, we fear that if we are not able to make selected promotions, we may lose productive members of the staff.

Fiscal Year 1972
Annual Report
General Research Support Branch
Division of Research Resources

Introduction

Under the aegis of its extramural research programs, the NIH has long recognized and supported the development of institutional biomedical research strength. Although primarily concerned with fostering categorical research efforts in its attack on the major health problems of this country, the NIH recognizes that the quality of individual research efforts is related to the quality of the institutions in which the research is done. These institutions provide the environment in which the research will be performed, and the milieu in which future faculty and research investigators obtain their education and research training. It is imperative, therefore, that institutions engaged in the education of health professionals and in the conduct of biomedical research have a vigorous and developing research life. Through the General Research Support Programs, the NIH provides non-categorical research grant funds to eligible institutions for the general support of health-related research and research training. The institutions determine at the local level what types of biomedical research and research training activities should be supported with GRS funds, so that their self-conceived goals and aspirations can be best achieved.

As the NIH categorical research and research training programs expanded, NIH realized that institutions that conduct categorical research in response to national needs could develop imbalances in their overall research programs, and that little if any local control could be exerted over the direction of growth that might result because of such national programs. Consequently, two grant programs were initiated in an attempt to restore appropriate institutional control over institutional research. These two programs are the General Research Support Grant (GRSG) and Biomedical Sciences Support Grant (BSSG) programs.

GRS funds have also been allocated for the development of new or enhanced capabilities at selected institutions. The Health Sciences Advancement Award (HSAA) program was the first program established for this purpose. This program was designed to assist certain health research institutions to join the ranks of the preeminent. With the phasing out of the HSAA project, another program was established in FY 1972. This program, initiated under the title Minority Schools Biomedical Support (MSBS) program, has the primary objective of strengthening the institutional research and research training capabilities of four-year colleges, universities, and health professional schools in which student enrollments are drawn mainly from ethnic minority groups.

GENERAL RESEARCH SUPPORT AND BIOMEDICAL SCIENCES SUPPORT GRANT PROGRAMS

General Research Support Grants (GRSG) (awarded to health professional schools, hospitals and other non-academic research institutions), and Biomedical Sciences Support Grants (BSSG) (awarded to non-health professional academic institutions) provide general support for health-related research and research training. Institutions use these awards according to their own best judgment of their needs, to support a variety of biomedical activities such as: pilot projects, including funding for the exploration of novel ideas; for young investigators; the development of research components of new programs and departments; research training programs; regular research; and for institutional biomedical research services and resources.

The fundamental rationale behind the GRSG/BSSG programs is that effective health research requires a strong institutional base of support. These programs serve to enhance the effectiveness of project research at the institutions and allow the institutions to redress imbalances and cultivate excellence in these research programs.

The GRSG/BSSG programs enable each institution to develop in ways not generally associated with project grants to individual scientists or with other types of research and training support. Through flexible funding of the GRSG/BSSG programs research institutions can change direction, start exciting new programs, and provide funds for fresh ideas and the scientific skill needed to tackle them, based upon the judgment of the institution's own administrators, with minimal direction and control exercised at the Federal agency level.

Fiscal Considerations

Extensive testimony has been received from many sources as to the immense value of the traditional formula General Research Support and Biomedical Sciences Support Grants. These grants provide their institutions that are heavily committed to mission-oriented project research, supported by NIH, with relatively flexible funds for the development of their biomedical research in accord with institutional objectives. The officials, however, are greatly concerned over the continuing downward trend of the size of the grants, and with the increasing costs of research activities, this unfortunate trend makes it more and more difficult to carry out the objectives of the program and aggravates the problems of their institutions, which are already faced with serious financial crises.

Except for FY 1970, which was the final phase-out year for 13 dental schools, the number of General Research Support Grant grantees has reached a new high of 339 in FY 1972 (Table I). The amount of available funds has not kept pace with the increase in number of grantees. As shown in Table I, in 1965 there were 66 less grantees than in 1972, with just a half million dollars less awarded compared to what was awarded in 1972. In 1968 with only 311 grantees $48.2 million was awarded, while in 1972 with 339 grantees only $44.3 million was awarded, a decrease of about $4 million.

TABLE I

Number Of Grantees By Type And Funds Available For The General Research Support Grant Program FY 1965 - 1972

Type of Grantee Inst.	FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972
Medicine	89	89	90	95	99	100	100	101
Dentistry	49	49	49	49	49	49	33	34
Osteopathy	5	5	5	5	5	5	0	0
Pub. Health	12	12	12	12	12	12	12	12
Pharmacy	5	5	9	10	12	15	15	16
Vet. Med.	11	9	13	15	17	17	17	16
Nursing	0	0	0	0	0	0	2	4
Hospitals	55	51	64	71	75	79	76	79
Health Dept.	3	3	3	3	3	3	2	2
Res. Inst.	44	41	49	51	58	64	69	75
TOTAL	273	264	294	311	330	344	326	339

Total General Research Support Grant Funds Awarded (In millions)

	FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972
Total Funds Awarded	$43.8	$39.2	$41.7	$48.2	$48.2	$45.8	$43.4	$44.3

Tables II and III show the distribution of the GRSG/BSSG's by size of the award. It can readily be seen that the number of grantees receiving smaller size grants is on the increase, and in 1972 the average size of the GRSG/BSSG's hit a new low. This is brought about by an increase in number of grantees, a relatively flat funding of the programs, and the overall increase in entitlement upon which the GRSG/BSSG formula is applied.

TABLE II

Distribution Of General Research Support Grants By Size Of The Awards

Size of Grant (in thousands)	Number of Institutions FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972
Under $ 30.0	23	14	22	27	30	49	34	46
$ 30 - 49.9	50	49	58	54	46	47	51	54
50 - 99.9	61	59	60	74	80	85	77	78
100 - 149.9	33	29	36	41	49	41	50	36
150 - 199.9	20	35	40	40	36	34	36	45
200 - 249.9	17	29	26	21	21	26	25	26
250 - 299.9	24	13	17	19	29	31	25	21
300 - 349.9	10	17	14	13	12	8	8	10
350 - 399.9	11	11	9	13	9	23	20	23
400 - 449.9	9	3	12	9	18	-	-	-
450 - 499.9	7	5	-	-	-	-	-	-
500 - 599.9	8	-	-	-	-	-	-	-
TOTAL	273	264	294	311	330	344	326	339

Grant Range (All Inst.)	Amounts (In thousands) FY 1965	FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972
Low	$ 11	$ 14	$ 14	$ 13	$ 12	$ 5	$ 11	$ 12*
High	585	459	441	424	429	396	383	367
Average	161	149	142	155	146	133	133	130
Number of Inst. Receiving Maximum Grant	4	5	6	7	7	10	17	21

* Represents award to an institution phasing out of the GRSG program. Lowest award for a fully funded grant was $20,725 in 1972.

TABLE III

Number of Biomedical Sciences Support Grants Awarded From 1966 Through 1970 By Size of Award

Size of Grants (in thousands)	Number of Institutions FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972
Under - $ 30.0	4	-	-	1	8	8	14
$ 30 - 49.9	36	32	27	36	35	36	36
50 - 99.9	47	54	60	59	59	57	59
100 - 149.9	3	6	11	11	9	9	5
150 - 199.9	1	1	3	2	2	1	2
200 - 249.9	-	-	1	1	-	1	1
Total No. of Grants	91	93	102	110	113	112	117
Total Amount Awarded (in millions)	$ 5.0	$ 6.0	$ 7.5	$ 7.5	$ 7.1	$ 6.7	$ 6.9

Grant Range (All Inst.)	Amounts (in thousands) FY 1966	FY 1967	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972
Low	$ 29	$ 33	$ 36	$ 29	$ 15	$ 12	$ 15*
High	160	179	219	220	199	210	212
Average	55	65	74	68	63	61	59

* Represents an award to an institution phasing out of the BSSG program. Lowest award for a fully funded institution was $28,598 in 1972.

Tables IV and V show that there has been a steady upward trend of entitlement for the GRSG and BSSG programs. (The entitlement figure, which is the base used to calculate the GRSG and BSSG awards, is the amount of research grants awarded by NIH and NIMH.) The GRSG entitlement base has increased six-fold since the start of the program in 1962 while the amount of money made available for the GRSG program has only doubled. In 1962, 18.5¢ was paid out for each dollar of entitlement. In FY 1972 a new low of 9¢ was paid and it is estimated that the FY 1973 President's Budget will result in a new low of 7¢ per dollar of entitlement. The same trend is reflected for the BSSG program, where in FY 1972 a new low of 5¢ was paid and it is estimated that the 1973 budget will provide only 3.8¢ per dollar of entitlement. For the period of 1962-1972 the GRSG entitlement has had an average growth rate of 16.438 percent while the GRSG funds have been limited to only a 8.277 percent growth rate with the funds reaching a peak in 1969. For the period 1966-1972 the BSSG entitlement had an average growth rate of 9.176 percent while the average percent of growth for the BSSG funds has been 5.550 percent.

These events have resulted in a downward trend in the average size of the GRSG and BSSG awards. Some of the awards may be becoming too small to achieve many

of the Program goals. If this downward trend continues the net effect is that GRSG/BSSG funds will be much less able to carry out the Congressional intention for which the two formula programs were launched, namely, to provide institutional funds of sufficient magnitude so that grantee institutions will have an opportunity to redress imbalances created by the funds awarded by the ten Institutes and NIMH.

TABLE IV

Trends in NIH/NIMH Research Grant Awards (Entitlements) and in General Research Support Grant Funds, FY 1962-1973 1/

Fiscal Year	NIH/NIMH Awards (Entitlement)	GRSG Funds Awarded	Ratio (%) GRSG/Entitlement
1962	$108,234,000	$20,000,000	18.48%
1963	192,408,000	30,000,000	15.59
1964	241,426,000	35,000,000	14.50
1965	286,832,935	43,985,365	15.33
1966	320,415,167	39,200,000	12.23
1967	354,893,188	41,700,000	11.75
1968	393,366,592	48,174,445	12.25
1969	441,064,040	48,200,000	10.93
1970	448,080,707	45,802,000	10.22
1971	430,721,426	43,423,000	10.08
1972	495,806,184	44,298,000	8.93
1973 (est.)	607,800,000	42,060,000 2/	6.92

1/ Previous Fiscal Year Awards Received From the NIH Institutes and NIMH by GRSG Awardees

2/ GRSG Funds Based on President's Budget.

TABLE V

Trends in NIH/NIMH Research Grant Awards
(Entitlements) and in BSSG Funds, FY 1966-1973 1/

Fiscal Year	NIH/NIMH Awards (Entitlement)	BSSG Funds Awarded	Ratio (%) BSSG/Entitlement
1966	$ 80,233,656	$ 5,000,000	6.23%
1967	87,564,767	6,000,000	6.85
1968	108,925,527	7,500,000	6.89
1969	119,007,903	7,500,000	6.30
1970	123,150,660	7,125,000	5.79
1971	122,385,049	6,777,000	5.54
1972	138,129,124	6,914,000	5.01
1973 (est.)	169,300,000	6,564,000 2/	3.88

1/ Previous Fiscal Year Awards Received From the NIH Institutes and NIMH by BSSG Awardees

2/ BSSG Funds Based on President's Budget.

When the GRSG/BSSG programs were initiated, the maximum appropriation level of general research support funds was established at 15% of the NIH/NIMH research grants level. Although the Senate and House Appropriations Committee Reports have time and again reaffirmed the Congressional intent that up to the 15% level be made available, this goal has never been reached. As shown in Table VI a high of 8.3% was reached in FY 1969. Since then the level has been steadily declining. In FY 1972 it declined to 6.1% and the decline will continue to 5.7% in FY 1973 (based upon the President's Budget which is $588,000 less than FY 1972). In addition to the GRSG/BSSG programs, the Health Sciences Advancement Award and Minority Schools Biomedical Support grant programs described in another section are funded from the same pool of funds. If new GRSG/BSSG grantees and new programs, such as the Minority Schools Biomedical Support program are added, there must be an increase in available funds.

Both the House and Senate Appropriation Committee suggested that NIH consider the desirability of direct appropriation for the General Research Support programs, which are becoming increasingly important to the maintenance of the institutional stability of the recipients, and also eliminate an unnecessarily complicated appropriation through the NIH Institutes. It is planned to have this accomplished for FY 1974.

TABLE VI

General Research Support Program
(Dollars in Thousands)

	Appropriated for NIH and NIMH Research Grants	If 15% were made available for GRS Programs	Amount made available for GRS Programs	Percent of available GRS funds to total
1966	$604,377	$ 90,657	$45,200	7.5
1967	681,197	102,180	51,700	7.6
1968	727,366	109,105	59,700	8.2
1969	729,230	109,385	60,700	8.3
1970	744,061	111,609	57,677	7.8
1971	765,510	114,827	54,200	7.1
1972	901,119	135,168	55,212	6.1
1973	964,469 2/	144,670 2/	54,624 1/	5.7 2/

1/ President's Budget

2/ Estimated

Program Evaluation

The effectiveness of the GRSG/BSSG funds can be exemplified by citing examples of the representative accomplishments recently reported by grantees (see Appendix A). The examples cited convey an impression of the scope, diversity, and quality of the activities undertaken with GRSG/BSSG funds. They also demonstrate how GRSG/BSSG-supported research is of interest and benefit to all the Institutes of the NIH, and attest to the relevance of the work in terms of national problems and priorities. Considered in toto, they are indicative of GRSG/BSSG's versatility and its accessibility in relation to grantee health research needs.

Administrative

During the past year a new Annual Progress Report and Expenditure Report was put into use for the GRSG/BSSG programs. The format and information that will be obtained from the new Progress Report will provide quantitative information which will allow staff to analyze and evaluate all the grants according to a common data and technical base and thus provide the basis for sounder program evaluation. The Annual Expenditures Report has been reduced to a one-page report with no supporting schedules; whereas the former Annual Expenditures Report had a total of eleven supporting schedules. Some of the former information obtained by supporting schedules is now obtained with the Annual Progress Report, but the overall reduction should greatly reduce the reporting burden of the grantees.

The last Annual Report stated that a study would be completed during the summer of 1971 concerning the policy of allowing GRSG/BSSG grantees to carry over at the end of the year funds equal to the award received for that year. The study was completed and the conclusion reached was that there should be no change in policy. It was found that grantees for the most part have the carryover funds either obligated; i.e., equipment on order, or have definite planned uses for the funds such as, allocating an investigator funds that go beyond the end of the grant year, saving for an electron microscope, etc. The new Annual Expenditures Report accounts for this type of planning under a caption called "Internal Commitments." The grantee community stated that the carryover feature was one of the most important in the program.

HEALTH SCIENCES ADVANCEMENT AWARD PROGRAM

The moratorium on new applications for Health Sciences Advancement Awards will result in complete phase out of the program by the end of 1974. In FY 1972 only four non-competing continuation awards were made to the following:

University of Kansas
Duke University
University of California, Davis
Rice University

The latter two schools received their final awards in FY 1972. Kansas and Duke will receive their final award in FY 1974, thereby fulfilling pre-existing commitments.

During FY 1973 it is planned to make site visits and to make an in-depth evaluation of the institutions that have completed the HSAA program.

MINORITY SCHOOLS BIOMEDICAL SUPPORT PROGRAM

The Minority Schools Biomedical Support (MSBS) program is a new initiative started in 1972, based upon the Senate Appropriations Committee Report, No. 92-316, July 29, 1971. The MSBS program is designed to strengthen the institutional health-related research and research training capabilities of four-year colleges, universities, and health professional schools in which student enrollments are drawn mainly from such ethnic minority groups as blacks, browns, (i.e., Chicanos, Puerto Ricans, Hawaiians, and other Polynesians), reds (American Indians), and orientals. The program is necessary in order that minority groups may have equality of opportunity to become investigators in biomedical research, and to become physicians, dentists, and other health professionals.

Specifically, the MSBS program will (1) enhance the biomedical research and training environment of minority academic institutions, (2) strengthen the faculties of minority academic institutions, (3) involve minority students in

research, (4) increase the number of minorities well-trained for health professional and graduate schools, and (5) provide funds for the support of exploratory research.

Fiscal Considerations

The program was funded for its first year at the $2 million level in 1972. Originally it was envisioned that only the 85 traditionally black colleges and universities would be included; since then, other ethnic minority institutions have been made eligible for the program. An additional 40 schools have been identified with student enrollments drawn mainly from ethnic minority groups. Of this expanded total of about 125 institutions, 95 are predominantly black, 18 are Chicano and Puerto Rican, 1 is American Indian, 2 are oriental, and 9 are composed of Hawaiian and other racial extractions.

The response from ethnic minority institutions to the December 1, 1971, announcement of the MSBS program was greater than anticipated. Seventy-five applications were received, seeking about $11.4 million for the first year of support. Of these, 42 were recommended for support by the National Advisory Research Resources Council (NARRC), 25 disapproved (mostly with advice), and six deferred for site visits, and two withdrawn.

The Council strongly recommended that the Division of Research Resources make seven-month awards for the first budget period so that a significant number of approved applications might be paid. If 12-month awards had been made, only 16 grants could have been funded from the $2.0 million available. Following through on the Council recommendation, seven-month awards were generally made. As a result, 38 MSBS programs were initiated in FY 1972, all but two of which have five-year project periods. Approximately $3.9 million of non-competitive funds will be required out of the $5.0 million in the President's Budget request for FY 1973, leaving about $1.1 million for competitive awards in FY 1973.

Program Evaluation

Because the MSBS awards were made effective June 1, 1972, no program evaluation based upon progress reports can be made for this report. The value of the MSBS program as it was conceived, and its perceptiveness in meeting a need at ethnic minority schools is clearly demonstrated by the extraordinary response (79 out of about 125 eligible institutions submitted a total of 75 applications within two months after the opening of the program).

The initial impact of the first awards can be measured from the following facts. The 38 awardee institutions are located in 18 states, the District of Columbia and Puerto Rico, and cover the nation from Hawaii to the Atlantic, from Illinois to the Gulf Coast. Only four of the awardees received research grant funds from NIH in FY 1971, thus clearly fulfilling one major objective--to open up research opportunities to minority institutions which had not been in the NIH competitive system. Almost 66% of the awards were made to four-year colleges, and about 8% to institutions awarding a science doctorate. Ethnically, 32 awards were made to predominantly black institutions, three to Chicano schools, and one each to an Indian, Hawaiian and Puerto Rican school.

The MSBS program is intended to provide research opportunities to faculty members who are currently restricted by very heavy teaching loads, and to provide research training for undergraduate as well as graduate students. The initial awards include support for research for 199 faculty members, and research training support for 282 undergraduates, 44 graduate students and one postdoctoral student (a total of 327 students). The coverage of this program is indicated by the fact that the number of student participants is almost 50% as great as the total number of Ph.D. scientists who are black, brown and red.

Since initiating the MSBS program, it has come to the attention of the General Research Support Branch that there are large numbers of Chicano, Puerto Rican, native American Indian, and Black students located at four-year colleges where they are not a majority. Under the current MSBS policy guidelines only institutions with a majority of ethnic minority students are eligible to compete. Therefore, large numbers of Chicanos and Indians are not able to benefit from the MSBS program as it is currently constituted. The same situation prevails in the northeast for Puerto Ricans and Blacks in areas such as metropolitan New York. If funds are made available it is planned to expand the MSBS program to include these clusters of minority students.

Administrative

Of the 75 MSBS applications that were reviewed, only 38 were site visited. This was caused primarily because of the limited staff available. The National Advisory Research Resources Council expressed concern that under existing employment allocations a skeleton professional staff—totally insufficient in number--is expected to be responsible for the administration of all four of the General Research Support Programs. In view of the Congressional mandate to mount a program having the design, purpose, and unique value of the Minority Schools Biomedical Support Program, the Council recommended that appropriate steps be taken to provide the Division of Research Resources with the necessary personnel for the effective administration of this program and the other three Branch programs, and a Resolution was adopted to that effect.

EXAMPLES OF REPRESENTATIVE ACCOMPLISHMENTS SUPPORTED BY GRSG/BSSG FUNDS

The most significant thrust of the GRSG/BSSG programs administered under the General Research Support authority is that the judgments and decisions regarding the uses of funds are made locally at, and by, the grantee institutions and therefore greatly assist the institutions in promoting and implementing those health-related research and research training activities which are most beneficial to their overall objectives.

The following examples are evidence of some flexible institutional programs that have resulted in significant contributions to the grantee institutions themselves and to biomedical science.

A. Biomedical Significance of Pilot Research Projects

1. The University of California, Los Angeles, reported that one of the most significant uses of the General Research Support Grant is the support of pilot research projects during that crucial period of data accumulation and evaluation prior to the submission of formal application for research support. Also, from a pilot study has come evidence that ceramic-coated denture implants, which have distinct advantages over the standard chrome-cobalt alloy type, may be used for routine replacement of lower teeth.

2. Sickle cell anemia research was one of several pilot research projects supported by GRS funds at the Lankenau Hospital during the last year. One purpose of this program was to determine a method of reactivating the production of fetal type hemoglobin, that is, to "switch" it back on to replace the abnormal adult hemoglobin. While the goal has not been achieved, this institution claims significant progress toward some day making it possible by means of "genetic engineering," to replace in an adult person the abnormal adult hemoglobin by the normal fetal type.

3. A pilot study to ascertain the incidence of lead poisoning in children of the city of Boston and to find those needing immediate treatment was supported under a GRS award. This small pilot study had important and far-reaching effects. Because of the information derived in this study, the officials of the city of Boston have provided staff and laboratory facilities so that each year blood lead concentrations can be measured in 50,000 children between the ages of one and five, and follow-up blood lead determinations will be made as needed.

4. A pilot study recently conducted by a University of Washington physician and supported by General Research Grant funds, may provide an important clue in determining the causation of rheumatoid arthritis, a debilitating disease which affects millions of Americans.

5. The University of Georgia College of Veterinary Medicine reported that GRS funds over the last few years helped support embryonic projects on immunity to Chagas' Disease and a virus-caused tumor, resembling Burkett's Lymphoma in man. Today these research activities are funded by NIH, the Department of the Army, and other outside agencies at a level exceeding $200,000 per year.

B. Establishment of New Research Tools and Capabilities

1. General Research Support Grant funds were used to establish the Materials Science Toxicology Laboratory on the Medical Units Campus of the University of Tennessee. This Laboratory has recently been designated as a clearing center for identifying the toxicity of plastic materials for the National Institutes of Dental Research. This unique facility thus serves the needs of the Federal (NIDR) program and American industry as well. Additionally, it has promoted interdisciplinary cooperation between the colleges of Dentistry and Pharmacy of the University.

2. The Biomedical Sciences Support Grant awarded to the University of Michigan's research program during 1970-1971 was used primarily for the purchase of a scanning electron microscope. Although the microscope has been in use only since early summer, 1971; it has served many needs of the university researchers in matters affecting human health. The instrument has been used extensively in research areas such as hearing, and for environmental contamination studies carried out in the Department of Environmental and Industrial Health of the School of Public Health.

3. One significant advance at the Evanston Hospital attributed to General Research Support has been the formation of a Coagulation Research Laboratory. This Laboratory has been able to accomplish a significant amount of research in relation to blood clotting disorders and their meaning in pre-surgical situations. Pre-surgical coagulation tests have been developed so that patients with apparent clotting disorders can be detected and not allowed into surgery until either the defect is compensated for or only after adequate supplies of materials have been made accessible to respond to anticipated crises.

4. Support totalling $120,000 from Biomedical Sciences Support grants was used at the University of Maryland from 1968-1972 to help equip and staff the Biochemistry Division. The major research activities of this new unit involve investigations of biochemical control mechanisms, and a study of the neurochemistry of biological systems that are relevant to such human health problems as cancer and neurological diseases. Other BSSG funds at this institution have been used to support the establishment of a Center for Language and Cognition in the Department of Psychology. The support of basic research activity in this area is geared toward the pursuit of knowledge about cognitive processes in causative, diagnostic and treatment phases of mental disorders.

5. At the Cancer Research Center in Columbia, Missouri, General Research Support has contributed significantly to the completion of a Detection Research Clinic. The clinic is designed to provide for: (a) mass screening for the detection of cancer, (b) a means to study and evaluate new methods of cancer detection (such as computerized history taking), (c) specialized biochemical testing, and (d) facilities for outpatient clinical research.

6. A large proportion of 1970-1971 GRS funds to the University of California at Berkeley was used to support a Statistical Research Service Unit. This new and enterprising capability has provided access to newer approaches in electronic data processing and has introduced an important tool for scientific research. The initiation and operational success of the Conversational Computer Statistical System (CCSS), which provides a direct link between the investigator and his data in a "conversational" mode, is an outstanding example of an activity of the Statistical Research Service Unit.

7. Funds from the General Research Support Grant were used at the University of Michigan Medical School to establish and support a laboratory for research on "Amniocentesis," a process which involves puncturing the mother's stomach, withdrawing the amniotic, water-like fluid which surrounds the fetus, and then using the fluid for various types of laboratory tests. This technique is used by the University of Michigan investigators primarily for the diagnosis of mongolism, a congenital disease with a high incidence of occurrence among children of older pregnant women. However this medical technique may also be used for other purposes, such as determining the sex of the child before birth.

C. Value of Flexible Institutional Support

1. The work of Dr. Earl Wilber Sutherland, Jr., winner of the 1971 Nobel Prize in physiology and medicine, was partially supported by the Health Sciences Advancement Award granted to Vanderbilt University.

2. The award of a General Research Support Grant to the Rand Corporation has made possible a number of health and biosciences studies during 1971. The health studies included work on national health insurance, state health manpower planning and consumer health care preferences. The biosciences studies included the development of models of various types of cancer chemotherapy and application of technology to problems of the visually handicapped.

3. The Long Island Jewish Medical Center stressed the importance of using GRSG funds to award small stipends for summer research fellowships to graduate students. The rationale offered is that during this time when research support opportunities are limited, the attractiveness of research as a future endeavor for young physicians and scientists has diminished. The opportunity to offer these small stipends for summer research training experience enables the Center to expose these individuals to the scientific environment and have them participate in scientific research, hopefully to help persuade some of them that scientific research is a worthwhile career.

4. Cornell Medical College used its General Research Support Grant in a variety of ways. These include: (a) salary support for full-time faculty, (b) support for general research services such as a central animal facility and a machine shop, (c) initial research funds for new faculty and for new projects, (d) summer research fellowship funds for medical students, and (e) support for students who wish to take a year's leave of absence from medical school to do research.

5. The College of Veterinary Medicine at Texas A&M University cited the value of GRS funds with which a research program was very rapidly initiated to investigate certain epidemiological factors pertaining to Venezuelan Equine Encephalomyelitis following the recent spread of that disease in the southern part of the United States. Funds from other sources were not readily available for such an initiative.

D. Significant Research Contributions in the Biomedical Sciences

1. Under support from the General Research Support Grant Georgetown University has been able to carry out research into the applications of infrared thermography, a process which can be used for measuring the temperature of various parts of the body without any contact and yet with extreme accuracy. Infrared thermography is being used at the Georgetown University Medical Center as a diagnostic tool for detecting such problems as malignant tumors and acute appendicitis.

2. General Research Support Grant funds were used by the Boston University School of Medicine to support Dr. Benjamin Kominer's work on heavy water as a chemical tool that may permit further analysis of the process of excitation and contraction in normal and diseased or injured muscle. The use of this system may provide a useful tool for analyzing and understanding more thoroughly ways in which normal and diseased muscle, including heart muscle, are affected by such drugs as digitalis and caffeine.

PROGRAM ANALYSIS BRANCH

The Program Analysis Branch collects and maintains on a regular basis a large volume of data relating to the four programs of the Division. The source documents for these data are applications, award statements, expenditures reports and annual reports. From this data bank, PAB produces annual and periodic publications such as:

(1) The "Research Resource Grants" booklet which contains highlights, graphs, highlight tables, summary tables and listings that pertain to the DRR grants and reflect the magnitude, scientific and technical diversity, geographical coverage, and general vitality of these programs of support for resources;

(2) A publication for the National Advisory Research Resources Council, "Division of Research Resources Handbook," which is a compendium of current and historical data on the appropriations and awards of the Division and its four programs, and which presents a brief description of the goals, objectives and general activities of the Division's programs;

(3) The General Research Support Program Awards History Booklet which lists the name, location, type of institution, grant number and amount of award for each recipient of general research support since the inception of the program in 1962, and includes summary tables by type of institution within fiscal year and by geographic division within fiscal year;

(4) A Biomedical Sciences Support Program Awards History Booklet which contains the same type of information for this program as described under (3) for the GRS program;

(5) The General Research Support Expenditures Booklet which shows the data over a six-year span as tabulated from the Annual Report of Expenditures filed by all recipients of General Research Support; the booklet includes summary tables for all types of institutions according to the type;

(6) A Biomedical Sciences Support Program Expenditures Booklet similarly constructed as that described in (5) above.

PAB is also in the process of developing and producing a "Division of Research Resources Basic Data Book" which will be a collection of highlighted DRR data and related facts in a pocket-size booklet.

The data system established by PAB for the Division contains approximately 309 data items which are defined and described in the PAB Handbook of Definitions and Specifications for the three distinct master files maintained, as well as in the documentation for the Publication Retrieval System master files. A completely computerized system has been established and, depending on the nature of the task, access to the data is accomplished through the 360/20 remote or the IBM 2741 Communication Terminal. Various methods are used such as computer programs, the Inquiry and Reporting System (IRS), and the Publications Retrieval System (PRS) which is similar to the Administrative Inquiry Reporting System (AIRS) introduced by the Division of Computer Research and Technology.

Presently a major effort is devoted to the restructuring of PAB's data capture and retrieval procedures to accommodate the revised forms for the Annual Report of the General Clinical Research Centers and the Report of Expenditures and Annual Report of the General Research Support grantees. A joint effort is also being instigated to review, edit and collect research project data from pages 2 through 5 of the GRS Annual Report on the IBM 2741 Communications Terminal in PAB. The research project data include the project title, name of investigator(s), amount of support and type of project. Guidelines for editing the reports and procedures for capturing the data are being written by the PAB staff. This system now under development will employ the Publication Retrieval System in a similar manner, as established last year for the GCRC Annual Report research projects, by using the WYLBUR text editing and remote job entry facility supported by the Division of Computer Research and Technology for keying in and editing of the data. PAB will coordinate the input activities, transfer the data to tape, maintain the tape files and be responsible for all facets of the project. With the system PAB can identify the scientific content of the GCRC research studies at various depths, including specific diseases, disciplines and techniques.

The PAB has also worked closely with the General Clinical Research Centers Branch in establishing criteria and processing appropriate data to be used in evaluating characteristics of the center's program and has participated in the development of the rationale and general scheme for the evaluation of the General Clinical Research Centers program.

PAB has written and now maintains and executes a series of computer programs and subroutines which calculate the GRS and BSS awards, punch the cards which are used to prepare the award statements by computer, and produce listings and tables which when xeroxed and reduced in size are bound and distributed as the Final GRS Awards Booklet. This publication shows for

each institution the grant number, name, type of institution, form of control, entitlement and a comparison of the newly calculated award with the amount awarded the previous year. The awards are presented by eligibility within type of institution and within each category arranged by size of entitlement, amount of difference between the new award and the previous year's award, percent of difference, amount of new award, and grant number. When the need arises, PAB adapts these programs and subroutines to produce experimental manipulation of the GRS and BSS data in order to analyze the effect of various alterations of the formula and the resulting impact on the BSS and GRS programs. Currently PAB is developing a taxonomy of the possible alternatives to the practicality of merging the GRS and BSS programs and is simulating by computer the effect these would have on the various grantee institutions in the programs.

During the past year the Program Analysis Branch has had 100 percent participation in training programs. The PAB staff is encouraged to take advantage of training for either professional or personal growth. This is possible because each member of the Branch realizes the value of training and is willing to carry additional responsibilities when a fellow staff member is taking a course.

The above exemplify some of the Program Analysis Branch efforts to meet the Division's requirements for data reporting and program evaluation as they fit into the decision making process. During the coming year PAB will continue to study the Branches' data needs in order to expand its data base for analysis.

"Softly, yet meaningfully, Miss Neal led us through an enlightening, but terribly disturbing hour which focused on six women suffering from such varied illnesses as breast and cervical cancer, a crisis birth, menopause, and the stresses prevalent in a woman's competing in a man's world."

Those were the words of a top New York television critic about one of the Information Office's communications projects this fiscal year. The documentary about which she wrote plus seven other varied activities offer prime examples of how the Information Office works to inform various publics about the programs of the Division.

"Life, Death, and the American Woman" was the title of the one-hour documentary to which Kay Gardella referred in the New York Daily News. It aired April 27 on the American Broadcasting Company television network. The Information Office started working very closely with the producer at the idea stage for this special. In conjunction with the General Clinical Research Centers Branch, it offered suggestions on content which were incorporated into the show. The Information Office helped to select the clinical research center program directors who were featured as medical experts. It made special efforts to help the producer dramatize with great accuracy certain major medical problems of women. As a result of office assistance, the clinical research centers of the Division became a nationwide stage upon which the producer could build a constructive report about the diseases of women and what research has learned about possible preventive approaches.

The office arranged for NIH's clinical research centers to receive billing next to the main title of the special. As participants, each of the Division's grantee program director experts and his institution received additional billing. At the end of the special, the Division received full credits.

Bernie Harrison of the Washington Star said: "It was an admirable hour in a field poorly covered up to now by TV."

The Pittsburgh Press reported: "Normally, watching a television program is not a life and death matter."

The Cincinnati Enquirer called the show a "Super Special" and said: "ABC-TV's 'Life, Death, and the American Woman' special Thursday night was one of the best TV documentaries in recent years."

The New York Daily News said: "Once in a while the ratings-minded television industry proves it cares about people."

United Press International said: "Medical and health problems faced by American women were detailed in a tasteful, informative, and gently poignant one-hour ducumentary on ABC-TV Thursday night."

The Boston Globe called it: "A fine documentary on the human side of illness."

And the American people proved that they cared about the show with an estimated viewing audience of 51 million.

Another television documentary which was an office project was shown on 165 TV stations of the CBS network March 5. The research activities on apes at the Yerkes Regional Primate Research Center were featured on "Animal World." Dr. Geoffrey H. Bourne, Director of the Center, was one of the human stars of the half-hour show, which was filmed in its entirety at Yerkes. Dr. Bourne and the Information Officer met in Hollywood to review the script and to record an on-the-air credit for NIH and its primate centers program. In addition, the Division and NIH got final credit in a highly favorable half-hour show that included many medical research activities with the world's largest collection of great apes.

The Information Office worked very closely with writer Charles Marwick of Medical World News as he fashioned a 5,000-word cover story for the magazine titled "Burgeoning Primate Centers - a new level of medical research." In addition to furnishing extensive background information, the Information Office made arrangements for him to interview Dr. Bowery, Division Director, and Dr. Goodwin, primate center program chief, on NIH involvement in the primate centers program. The Information Office arranged for Mr. Marwick to visit the Yerkes and New England Primate Research Centers in order to learn first-hand about their work. Extensive quotes from Drs. Bowery and Goodwin appeared in the article together with many details on the Yerkes and New England Centers.

While the Information Officer and Assistant Information Officer were in California on another project, they interviewed and photographed Dr. Earl Collard, Assistant Professor of Dentistry at the University of California at Los Angeles. Dr. Collard's research project, hearing through the teeth, was funded under the Division's General Research Support Grant Program. The idea behind Dr. Collard's project was to develop a more efficient way to hear sound through a magnetic or crystal transducer inserted in a false tooth. The Assistant Information Officer alerted the Newspaper Enterprise Association to this story with a fact sheet and pictures. Dave Hendin, editor of Enterprise Science Service, worked with Dr. Collard in developing a 1500-word feature on his work, which acknowledged Division of Research Resources support, and utilized pictures provided by the Division. Thus far, this story has run in over 100 newspapers with a combined circulation of over 2 million.

A filmstrip on the Division and its five programs was in the final stages of production as the fiscal year came to an end. Using a unique documentary style, it was shot and taped on location at four Division-supported resources and at the locale for two General Research Support Grants. Scientists "told it like it was" for still cameras and recorders. When the show is complete, the viewer will be able to see the actual day-to-day work of the resources through the eyes of the director and individual scientists. Dr. Bowery is host/narrator for the 25-minute show, which was slated for release in June.

Three exhibits were produced for the Animal Resources Branch by the Information Office. The first, "NIH Laboratory Animal Resources," made its debut at the FASEB meeting in Atlantic City. It featured giant blow-ups of pictures from the Johns Hopkins Animal Resource, which were shot for the Division filmstrip

series. The Assistant Information Officer, who manned the exhibit, estimates that at least 1500 attendees either viewed or stopped at the eye-catching display. The regional primate research centers were featured in two additional exhibits: a table top show that was shipped to the Third Congress of Experimental Medicine and Surgery in Primates at Lyon, France, and a full-scale primate centers exhibit for the Fourth International Congress of Primatology at the Oregon Regional Primate Research Center, Beaverton, Oregon, in August.

Last December, the Information Office launched the Minority Schools Biomedical Support program press campaign. It initially consisted of a carefully prepared information kit sent to over 300 selected newspapers, magazines, and broadcast stations. The kit contained:

Release on the MSBS program
Background information
Feature story on Virginia State College
Photos of black scientists
MSBS Guidelines

Follow-up telephone calls were made by the Assistant Information Officer to selected major media.

The release was carried on the Associated Press wire and appeared in the New York Times. A MSBS feature was also distributed on Enterprise Science Service (700 newspapers) in January. Some of the professional publications carrying the announcement were the Washington Report on Medicine & Health, Drug Research Reports, FASEB Newsletter, DRG Newsletter, HEW Newsletter, NIH Record, Bulletin - National Society for Medical Research, and the Biomedical News.

In December, a radio interview was arranged by the Information Office with the Black Audio Network. This five-minute interview with Drs. Gibbs, Alexander, and Willis was carried by 100 black radio stations throughout the country.

A follow-up release was distributed in April, and drafts were being readied for a news release on the first awards in May.

One DRR official commented that every black college he visited had either seen the announcement of the program or heard about it, as an indication of the depth of the MSBS coverage.

Finally, in the category of the little noticed, everyday concerns, it is interesting to note that the Information Office answered, mostly by mail, over 700 requests from people for program information from January through April.

These eight activities were selected to show the span of office work during the year. This report does not address itself to many other individual placements or projects, too numerous to mention, which the office was involved in during the year.

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